Orthokeratology, binocular co-ordination and myopia control

The influence of baseline accommodation and binocular vision on myopia progression control and the impact of myopia progression control on accommodation and binocular vision.

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Abstract

This work investigates two key questions: ; how myopia progression control treatments impact accommodation and binocular vision function and if accommodation and binocular vision function prior to myopia control interventions has any association with the efficacy of treatment. The work is made up of four main studies.

Study 1 was a review and re-analysis of a previously completed study to investigate whether there are any possible associations between accommodation and binocular vision status prior to lens wear which may impact the myopia control efficacy of orthokeratology lens treatment. The data of 26 children were used. The study involved using an orthokeratology lens in one eye, with the contralateral eye used as a rigid gas permeable lens wearing control. Given the unusual nature of this modality, accommodation and binocular vision status was measured at baseline and monitored throughout the study to ensure that there were no adverse responses to lens wear. In a novel analysis of pre-existing data, the accommodation and binocular vision profiles of those participants that responded the best to orthokeratology lens treatment in terms of inhibiting ocular axial length growth were compared to those that did not respond to treatment. A similar comparison was made between those participants who progressed the most to the least in the control eye.

Results from this analysis suggested that accommodation and binocular vision status prior to orthokeratology lens wear may be associated with treatment effect. Orthokeratology lens treatment worked best for myopia control when accommodative facility was higher and closer to population norms, AC/A ratio was lower and closer to population norms and accommodative lag was higher. None of these associations reached statistical significance, however further investigation appeared warranted.

Interestingly, baseline near phoria did not appear to have an influence on response to treatment with orthokeratology lens wear. This is different to bifocal spectacle lens wear studies that show that initial near phoria has an impact on the efficacy of myopia control treatment.

Study 2 was a review of clinical records of 37 children and young adult patients seen in two private optometric practices in Australia. Accommodation and binocular vision function prior to orthokeratology lens wear was compared to during lens wear in patients who were fitted with orthokeratology lenses between 2010 and 2012.

The results of this study showed that there was a statistically significant change in mean near phoria in the exo direction with lens wear. Mean positive relative accommodation increased, mean negative relative accommodation decreased and accommodative facility increased. While the mean distance phoria remained unchanged there was a statistically significant reduction in the standard deviation of this variable. There was a slight reduction in mean lag of accommodation, but it failed to reach statistical significance.

The study showed that the binocular vision status including accommodative and vergence measures changed during orthokeratology lens wear. The changes were in a direction closer to population norms.

Study 3 was a prospective study of the impact of short-term orthokeratology lens wear on binocular vision in 12 young adults. Measurements of binocular vision status were taken at baseline and after one month of lens wear.

The results of this study were similar to Study 2. There was no statistically significant change in mean near phoria. Distance accommodative facility increased. There was a slight, but not statistically significant, change in mean near accommodative facility.

Again, while there was no change in mean distance phoria, there was a significant reduction in the standard deviation of this variable.

Additional variables of interest in this study included stereopsis, which was unchanged, and fixation disparity at distance and near which were unchanged.

This short-term study showed that orthokeratology lens wear alters binocular vision status including accommodative and vergence measures. Again, the changes in binocular vision were in a direction closer to population norms.

Study 4 was a record review of patients seen in the Myopia Control Clinic at the University of New South Wales, Sydney, Australia. The accommodation and binocular vision function of myopic children treated with orthokeratology lens wear or low dose atropine were reviewed. A total of 9 children treated with orthokeratology were followed for 3 to 6 months. Mean near phoria moved in the exo direction with orthokeratology lens wear and gradient AC/A ratio moved to more normal values with lens wear. There was an association between annualised axial length growth and gradient AC/A ratios and stereopsis, suggesting that baseline accommodation and binocular vision function may influence treatment.

A total of 19 children were treated with low dose atropine and data were available from 3 to 6 months of treatment. Low dose atropine led to a small but not statistically significant decrease in amplitude of accommodation. Patients who were the worst responders to low dose atropine had lower baseline amplitude of accommodation compared to the best responders. Although speculative, the reduction in amplitude of accommodation may have a detrimental impact on the accommodation and binocular vision function and increase blur. Alternatively, those patients with high amplitude of accommodation may benefit from a subtle change in the accommodation and vergence relationship.

Both accommodation and vergence measures of binocular vision status appear to change with orthokeratology lens wear. The changes in binocular vision move in a direction closer to population norms; this is a novel finding of this thesis and is not reported elsewhere. Binocular vision that is abnormal has been associated with onset of myopia and progression. The changes in binocular vision associated with orthokeratology lens wear may contribute to the myopia progression control effect. Close monitoring of accommodation and binocular vision during myopia progression treatment is warranted.

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1 Background

This chapter gives an overview of the eye, vision function, and refractive errors including myopia and its control. A list of acronyms and symbols (Appendix A, p. 211) and glossary of terms (Appendix B, p. 213) can be found in the appendices of this thesis. Chapter 3 includes full descriptions of accommodation and binocular vision tests.

1.1 The eye and vision

Light enters the eye and is focussed on the retina by the cornea, an avascular collagen tissue and the crystalline lens, a flexible, avascular collagen tissue attached to the ciliary muscle via fibres called zonules (see Figure 1-1). The light focus can be varied by changes in shape of the crystalline lens with muscle contraction and relaxation. This ability of the eye to alter focus is called accommodation. At the retina light reacts with photosensitive pigments in retinal cells (rods and cones) and is converted into a neuronal action potential. This is carried through the visual pathway via ganglion cells in the retina, through the optic nerve and via synapses into the areas of the brain associated with the perception of vision. The amount of light entering the eye is controlled by the pupil.

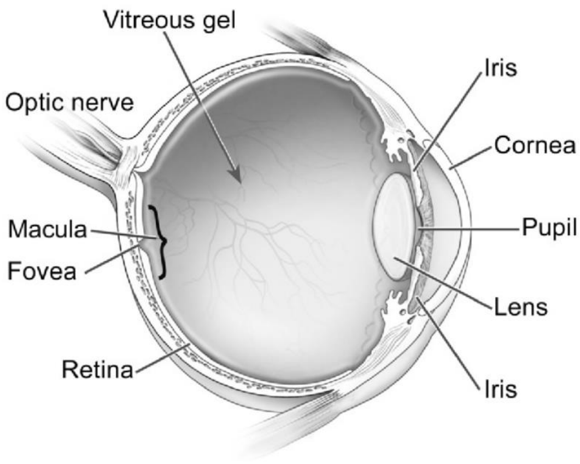

Figure 1-1 Human eye in cross-section (image from National Eye Institute, National Institutes of Health).

Helmholtz first described the mechanism of accommodation in 1855. When focussing into the distance the ciliary muscle relaxes. This induces tension on the lens zonules which causes the lens to flatten. When focussing on near objects the ciliary muscle contracts. This releases the tension on the lens zonules which causes the lens to steepen (Glasser and Kaufman, 1999).

Accommodation is greatest in infants and decreases with age due to hardening of the lens which reduces its ability to change shape. The parasympathetic nervous system controls accommodation but there is some evidence suggesting sympathetic inhibition (Mallen *et al.,* 2005).

Eye movement is controlled via six extra-ocular muscles with neural input from the cranial nerves III (Oculomotor), IV (Troclear) and VI (Abducens). Co-ordination of the muscles and neural integration is required for single binocular vision (Evans, 2007). The binocular vision system can break down resulting in eye misalignment (strabismus) or lazy eye (amblyopia). Strabismus and amblyopia occur in approximately 4% of the population. This thesis will not be addressing strabismus and amblyopia. Less extreme binocular vision abnormalities occur more commonly in approximately 20% of the population consulting optometrists (Karania and Evans, 2006).

Accommodation, vergence and pupil size are all closely integrated. When looking at a near object the three responses of accommodation, inward movement of the eyes (convergence) and pupil constriction are activated, with the opposite occurring (divergence and pupillary dilation) with distance viewing.

At birth, eyes are approximately 70% the size of adult eyes. Their growth is regulated by genetics and environmental influences including visual stimuli (Wallman and Winawer, 2004) in order to maintain clear vision. By six years of age most eyes are without refractive error (emmetropic). This process, called emmetropisation, occurs with the optical components of the eye including the cornea and lens altering shape to match the growth in axial length (the distance from the cornea to the retina). Throughout childhood eyes continue to grow, with axial length increasing by approximately 0.1mm per year in emmetropic children (Mutti *et al.,* 2007). When there is an imbalance between the eye's focussing power and the length of the eye, the result is called refractive error. Refractive error can be categorised as myopia, (near-sightedness), hyperopia (farsightedness) or astigmatism.

1.2 Myopia

Myopia occurs when the axial length of the eye is too long for its optical components to focus distant objects clearly on the retina, leading to clear near vision with blurred distance vision. The most common form of myopia begins in childhood and increases until the middle or late teens. The age when ocular axial length growth ceases is similar to the age when adult height is reached (Goss *et al.,* 1990).

Myopia can be temporarily corrected with spectacles or contact lenses to refocus images onto the retina. Laser refractive treatment removes tissue from the cornea to alter its shape and refractive power to focus images on the retina.

Myopia is a commonly occurring eye disorder with increasing prevalence in countries around the world (Holden *et al.,* 2016). Logan and colleagues (2005) found 50% of first year university students in the UK were myopic. In the USA 33% of the adult population was reported myopic (Vitale *et al.,* 2008), an increase of 66% from the 1970's (Vitale *et al.,* 2009). In East Asia myopia is particularly prevalent. For example, in Hong Kong 37% of school children were reported as myopic (Fan *et al.,* 2004) and in Taiwan 84% of 16 to18 year olds were myopic in a report from 2001 (Lin *et al.,* 2001). This was an increase from 74% in a similar study reported 1983 (Lin *et al.,* 2004).

Myopia costs both the individual and society not only in terms of the need for correction with spectacles, contact lenses or laser refractive treatment but also lost employment opportunities. Rose and colleagues (2000) found that those with a high degree of myopia reported that there were psychological, cosmetic, practical and financial effects on their quality of life similar to those who have other serious sight threatening diseases such as keratoconus. High myopia is also associated with a greater incidence of cataract and greater risk of sight threatening diseases such as glaucoma, retinal detachments, chorio-retinal atrophy, myopic macular degeneration and lacquer cracks (Saw *et al.,* 2005).

How myopia begins and develops in an individual human eye remains relatively unclear despite great research effort. Multiple risk factors both modifiable such as lifestyle and environment and non-modifiable genetic factors have been identified. The mechanism for eye growth and subsequent myopia development is undoubtedly very complex. Treatment for myopia progression includes optical corrections, environmental modifications (including increased time spent outdoors) and pharmacological agents. This thesis will primarily focus on the role of maintaining clear vision through the eye focussing (accommodation) and eye co-ordination (binocular vision) systems.

Blurred vision resulting from optical defocus has been implicated as a regulator of eye growth in multiple studies in both humans and animals (Wallman and Winawer, 2004). There have also been numerous studies on different methods of optical correction and their ability to control myopia progression dating back to the early use of spectacles. Daza de Valdes noted that lenses for myopia correction should not be so powerful as to cause a perceived reduction in image size in his textbook of optics, ocular anatomy and the use and fitting of spectacles in 1623 (cited in Goss, 2003).

Optical corrections include under-correction, bifocal spectacles, progressive addition spectacles and contact lenses, and orthokeratology contact lenses.

Several variations to optical correction have been used in an attempt to reduce the progression of myopia with varying success. The use of spectacles that have been under-corrected for the level of myopia has been found to increase the rate of myopic development (Chung *et al.,* 2002).

Bifocal and progressive addition spectacle lenses which reduce the demand for accommodation with close work have been used for myopia progression control for several decades (Mandell, 1959). Bifocal and progressive spectacle lens trials have had varied results, however greater treatment effects were found in sub-groups of participants; those with esophoria at near viewing (Fulk *et al.,* 2000, Hasebe *et al.,* 2008) and with increased lag of accommodation (Hasebe *et al.,* 2008) and a combination of esophoria and increased lag of accommodation (Gwiazda, 2004). A recent review of myopia control treatments suggests that the myopia progression control effects are small and are of questionable clinical value (Walline *et al.,* 2011).

Early studies of the use of contact lenses that were made from rigid materials found they slowed myopia development (Morrison, 1960, Stone, 1973, Grosvenor, 1991 cited in Walline *et al.,* 2004, Khoo *et al.,* 1999). However, more recent studies by Katz and colleagues (2003) and Walline and colleagues (2004) have shown that myopia is not significantly reduced with rigid gas permeable contact lenses. The difference in the level of myopia progression in earlier studies was possibly due to corneal curvature changes associated with rigid contact lens wear (Walline *et al.,* 2004). Early studies with soft contact lenses showed an increase in the rate of myopia progression (Fulk *et al.,* 2003, review in Gwiazda, 2009). However other studies have shown that the rate of myopia development was the same as with spectacles (Horner *et al.,* 1999, Walline *et al.,* 2008). This may be a result of the different subjects studied, the design of the contact lenses or the methods used to determine eye growth.

1.3 Orthokeratology

Orthokeratology is the application of specially designed, rigid gas permeable contact lenses to temporarily correct myopia and other refractive disorders. Orthokeratology has been used as a form of optical correction since the 1960's. More recently, improvements in the measurement of corneal topography and in manufacturing technology has led to new more stable fitting lens designs which have resulted in better clinical outcomes (Swarbrick, 2006). Orthokeratology temporarily reshapes the cornea (Jessen, 1962). The use of improved contact lens materials with greater oxygen permeability has led to the use of the orthokeratology lenses overnight with lens free, clear vision during the day (Swarbrick, 2006).

There is a growing body of evidence that orthokeratology lens wear may slow the progression of myopia in some individuals (Reim *et al.,* 2003, Cheung *et al.,* 2004, Cho *et al.,* 2005, Downie and Lowe, 2009, Eiden and Davis, 2009, Lotoczky and Morgan, 2009, Ruskiewicz, 2009, Walline *et al.,* 2009, Cho and Cheung, 2010, Okada *et al.,* 2010, Kakita *et al.,* 2010, Lee and Cho, 2010, Okada *et al.,* 2010, Wilcox, 2010, Cho and Cheung, 2012, Swarbrick *et al.,* 2015).

1.4 Impact of myopia and role of optometry

The recent growth in the prevalence of myopia worldwide has caused many in eye care to be concerned and question the current prescribing of optical devices and recommendations for visual hygiene. Community optometrists have an important role in identifying those at risk of developing myopia and recommending strategies to reduce risk prior to development as well as managing myopia in ways that do not contribute to progression.

Little is known about the effect of wearing orthokeratology lenses on accommodation and binocular vision status and there are currently no studies that address whether the accommodation and binocular vision characteristics prior to lens wear influence myopia control outcomes.

1.5 Atropine

Over the course of completing this thesis low dose (0.01%) atropine has been introduced in Australia as a method of myopia progression control. It is currently a popular method of treatment in the University of New South Wales (UNSW) Myopia Clinic. This has led to the opportunity to extend an interest in the association of accommodation and binocular vision functions and treatments for myopia progression. Further background of atropine treatment can be found in Chapter 7.

This work investigates two major areas of interest; the impact of myopia progression control treatments, principally orthokeratology, on accommodation and binocular vision function and whether accommodation and binocular vision function prior to the myopia control interventions of orthokeratology and low dose atropine has any association with the efficacy of treatment.

2 Literature review

2.1 Overview

This thesis investigates two key questions:

- if accommodation and binocular vision function prior to myopia progression control interventions has any association with the efficacy of treatment and
- how myopia progression control treatments impact accommodation and binocular vision function.

As changes in accommodation and binocular vision function may, in some part be responsible for the myopia progression control effects seen in treatments this literature review was carried out to better understand any possible role of accommodation and binocular vision on myopia onset and progression. This part of the review also helps to identify what changes in accommodation and binocular vision can be expected with myopia development without treatment.

As previous studies have shown that baseline accommodation and binocular vision status influences the efficacy of myopia control a review of current optical correction for myopia control is included. The current understanding of changes to accommodation and binocular vision functions with myopia control treatments including orthokeratology was reviewed. There is a section on current theories of how orthokeratology lenses produce their treatment effect and includes some evidence of the limitations of these theories.

The aim of this literature review is to:

- Review the evidence of the association of accommodation and binocular vision with the onset and progression of myopia (onset and progression will be treated separately, because it is possible that different factors influence the onset and the progression of myopia)

- Review optical correction for myopia progression control
- Review the literature on the impact of orthokeratology on accommodation and binocular vision function
- Review the literature on the use of orthokeratology as a form of myopia progression control.

2.2 Method

A review of the English language ophthalmic, optometric and vision science literature was undertaken via the internet using the Medline database, the Google search engine, conference proceedings and other contact lens and optometric journals. Optometric journals not listed in Medline were individually searched via the internet. Additional publications searched included *Contact Lens Spectrum,* (www.clspectrum.com) and Optician (www.opticianonline.net).

The following search terms were used: myopia control, orthokeratology, corneal refractive therapy, accommodation, binocular vision, peripheral refraction. The reference list from each of the papers was also examined to determine other suitable papers.

The most recent electronic searches were carried out on 16th June 2017.

Studies not included in this review include several articles identified on orthokeratology and myopia control were case studies of a small number of subjects (Cheung *et al.,* 2004, Downie and Lowe, 2009, Lotoczky and Morgan, 2009, Ruskiewicz, 2009, Lee and Cho, 2010, Wilcox, 2010). Perhaps not surprisingly all these studies showed a positive effect of myopia control with orthokeratology lens use. Although these articles are of clinical interest they will not be included in this review due to the small number of cases, the use of subjective measures to determine myopic development, myopia not following a linear progression, no controls for comparison, the potential bias of the practitioners and the bias for publication of positive results. A retrospective review of orthokeratology lens wearing patients was carried out in Japan (Okada *et al.,* 2010) and presented as a poster at the Association for Research in Vision and Ophthalmology meeting. Although they reported that those under 18 years of age did not show any change in refractive error over a five-year period they do not report on the number of patients who were in this group. This study was also not included in the review.

2.3 Accommodation and binocular vision function and myopia

Several accommodation and binocular vision functions have been assessed in relation to myopia development and progression. These include measures of accommodation such as accuracy of accommodation (lag of accommodation), accommodative facility (responsiveness of accommodation), positive and negative relative accommodation (ability to change accommodation without changing eye alignment), eye alignment measures such as heterophoria (phoria), and combined responses such as the accommodative convergence to accommodation (AC/A) ratio. These functions will be considered in turn, with the possible associations with the onset of myopia and, once myopia has started, in the progression of myopia discussed.

A table summarising the findings of this section can be found in at the end of this section (p. 45) .

A review of common accommodation and binocular vision tests can be found in Appendix C.

2.3.1 Accuracy of the accommodative response (lag of accommodation)

During near vision accommodation is not precisely set at the same distance as the target, but instead typically lags behind the target. This error is called lag of accommodation. The accommodative lag is considered to be due to errors in the neural integrator in the accommodation control system (Schor *et al.,* 1986). The typical accommodative lag is so low that it is unlikely to impair visual performance (Nakatsuka *et al.,* 2005)

2.3.1.1 Predicting onset of myopia

Goss (1991) conducted a record review of patients seen in private practices in the USA. Patients were aged between six and 15 years of age. For analysis in this study they were grouped as “remained emmetropic” or “became myopic”. Lag of accommodation was measured using the binocular fused cross cylinder technique. Patients who became myopic were shown to have a higher lag of accommodation (mean +0.75D ± 0.41D) compared to those who remained emmetropic (mean +0.53D ± 0.43D).

Drobe and deSaint-Andre (1995) conducted a review of clinical records of 50 patients seen in private practice in France. Twenty-five patients who became myopic in a two-year period were matched with controls. Lag of accommodation was higher in patients who became myopic compared to those who remained emmetropic.

Gwiazda and colleagues (2005) followed 80 emmetropic children aged six to 18 years over three years. During this time 26 became myopic. They reported an increase in accommodative lag in pre-myopic children (mean age at first visit 11.1 years) two years before the onset of myopia. Accommodative lag was measured using a Canon R−1 infrared open field-of-view autorefractor (Canon Europa NV, Amstelveen, The Netherlands) with a testing distance of 33cm.

In contrast, Mutti and colleagues (2006), in a large longitudinal study called the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE), assessed a sub-set of 568 children who met strict refractive criteria for accommodative accuracy. They found that monocular lag of accommodation using a 2.00D and 4.00D Badal accommodative stimulus with habitual refractive correction was not found to be significantly different in those who became myopic compared to those who remained emmetropic. Comparable results were found for a near monocular target at 25cm. A higher lag of accommodation was seen after the onset of myopia.

Zadnik and colleagues (2015) evaluated a subset of participants from the same CLEERE study. A total of 414 children (mean age on entry to the study 6.7 ± 0.5 years) who were emmetropic but became myopic through the course of their study were included. They identified 13 potential predictors of the development of myopia including the binocular vision/accommodation measures of AC/A ratio and lag of accommodation. Univariate analysis showed that lag of accommodation was not an independent risk factor for the development of myopia.

2.3.1.2 Predicting progression of myopia

An increased lag of accommodation was correlated with myopic progression in six to 18-year-old participants (Gwiazda, 1995). A study by Abbott and colleagues (1998) stimulated accommodation in three ways; by a real target at varying distances, a distance target viewed through lenses with increased minus power and a near target viewed through positive powered lenses. They showed a reduced accommodation response to minus lens-induced accommodative demand in progressing myopes compared to those who were stable myopes. There was no difference in accommodation response between stable early onset myopes, late-onset myopes and emmetropes.

Rosenfield and colleagues (2002) followed a group of 23 young adults (mean age 23.0 years, ± 0.30 years standard error of the mean) for 12 months. They assessed accommodative response curves and lag of accommodation. Accommodative lag was measured using an open field autorefractor (Canon R−1 Optometer) with a letter chart viewed binocularly. They found that a low lag of accommodation at a 2.50D working distance was associated with increased myopia progression.

Allen and O'Leary (2006) noted that lag of accommodation (and poor accommodative facility) were predictors of myopic progression. However, this was an unusual sample in that the age was 18 to 22 years and 12 of the 30 myopes were late onset myopes.

Price and colleagues (2013) reported that AC/A ratio and lag of accommodation were significantly correlated to myopia progression. In their study, accommodative lag was improved either with the use of soft contact lenses which altered spherical aberration and therefore depth of focus, vision training or a combination of the two. Results were compared to a control group. By improving accommodative lag with contact lenses, they found that there was a reduction in myopia progression in patients younger than 16.9 years. However, this effect was only in the first year and as there was a more rapid change in refraction in the second year the final refractive error was the same as in other groups.

Weizhong and colleagues (2008) measured the lag of accommodation in 62 children (mean age 10.81 ± 1.60 years) with myopia (mean −1.70D ± 0.76D) in China. Accommodative lag was measured at 33cm using an open field autorefractor. They did not find a significant correlation between near lag and myopia progression.

A more recent longitudinal study followed 592 children in the USA who had been myopic for one year (mean age 10.4 ± 1.8 years) with mean spherical equivalent refractive error of −2.13D ± 1.24D. The children were from a mix of ethnic backgrounds including African American, Native American, Asian, Hispanic and Caucasian. They were fully corrected and lag of accommodation was measured at baseline and after one year. Lag of accommodation was measured monocularly using a 4D Badal accommodative stimulus. Neither of the measures were correlated with annual myopia progression ($p = 0.12$) (Berntsen *et al.,* 2011).

2.3.1.3 Accuracy of accommodation during myopia

A study of sixty-four five to 17-year-old (mean age 11.7 years) children showed the 16 myopes (refraction mean −1.94D, range −0.50D to −6.25D) had less accurate accommodation compared to emmetropes when viewing real targets at near. Myopes were also less able to increase accommodation when negative lenses were introduced in front of a distance target compared to emmetropes. Myopes viewing a near target and relaxing accommodation with positive lenses had an accommodative response that was similar to emmetropes (Gwiazda *et al.,* 1993). For their study myopes were fully corrected and not in their habitual correction and targets were viewed monocularly via an infra-red reflecting mirror in a Canon autorefractor (not open field).

Wolffsohn and colleagues (2003) found that late onset myopes have a significantly less accurate accommodative response at 4.50D demand than early onset myopes or emmetropes.

In a study of 61 myopic children (mean age 9.5 ± 1.3 years) Nakatsuka and colleagues (2005) measured the accommodative response under binocular conditions. They tested binocularly as they noted that the accommodative response is influenced by heterophoria measurements. They also compared the results for myopes when fully corrected and wearing their habitual correction. Myopic children showed larger lags of accommodation compared to emmetropes when fully corrected, however the lag of accommodation decreased when wearing their habitual correction. The average under-correction was significant (−1.40D ± 0.47D for the right eye). Lag of accommodation was measured using an open field autorefractor (Grand Seiko, Japan).

Early onset myopes demonstrated statistically significant greater near-work induced transient myopia at far than late onset myopes. Late onset myopes had greater near-work induced transient myopia than emmetropes. Interestingly the results were also impacted by the level of cognitive demand, with active cognition at near followed by passive cognition at far having greater persistence of near-work induced transient myopia.

In summary, studies of lag of accommodation measures showed varied results in the ability to predict both onset and progression of myopia. The lack of consistency with lag of accommodation in predicting onset or progression of myopia may be due to the lack of consistency in the testing methods used, the age of participants, and accommodative demand. Lag of accommodation has been shown to vary when tested monocularly or binocularly, with the testing method, testing distance and with age. In addition, the accommodative response is influenced by heterophoria measurements (Schor, 1999, Nakatsuka *et al.,* 2003).

Another source of variation for predicting progression of myopia is whether testing was carried out with full correction or while wearing habitual correction. Nakatsuka and colleagues (2005) reported that myopic children showed larger lags of accommodation compared to emmetropes when fully corrected, however the lag of accommodation decreased when wearing their habitual correction.

2.3.2 Distance and near heterophoria

2.3.2.1 Predicting onset of myopia

Goss (1991) conducted a record review of patients seen in private practices in the USA. Patients were grouped as “remained emmetropic” or “became myopic”. A total of 61 patients who became myopic were compared with 61 patients who remained emmetropic. Near phoria was tested using the Von Graefe method through the maximum plus distance binocular subjective refraction lenses. Patients who became myopic tended to have a more esophoric near phoria (mean 1^{Δ} esophoria ± 6 $^{\Delta}$) compared to those who remained emmetropic (mean 2^{Δ} exophoria ± 6^{Δ}) (Figure 2-1).

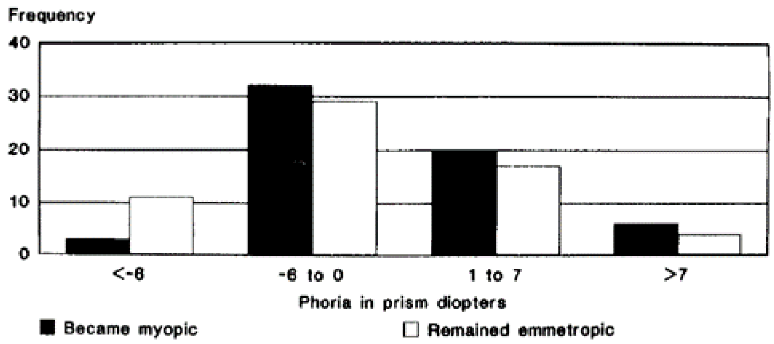

Figure 2-1 Frequency distribution of nearpoint phorias in prism dioptres. Negative values indicate exo and positive eso (from Goss, 1991).

Drobe and deSaint-Andre (1995) conducted a similar review of clinical records of 50 patients seen in private practice in France. Twenty-five patients who became myopic in a two-year period were matched with controls. Pre-myopes had an esophoric tendency when viewing near targets (mean 0.6^{Δ} esophoria ± 6.8^{Δ}) compared to stable emmetropes (mean 2.3^{Δ} exophoria ± 4.2^{Δ}) although there was large variation in results.

Goss and Jackson (1996) studied a group of 87 children over three years. Twenty-nine of these children became myopic during the study while 59 remained emmetropic. They noted that the presence of a near phoria that is outside of the range of 1^{Δ} esophoria to 3^{Δ} exophoria (or close to orthophoria) was a risk factor for the development of myopia (Figure 2-2). They found that the near phoria became more convergent (esophoric) with myopia.

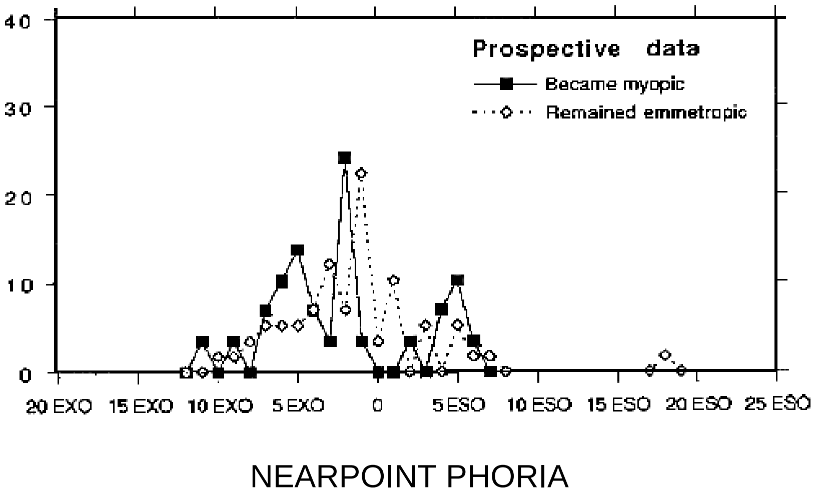

Figure 2-2 Frequency distribution of near phorias in participants who became myopic compared with those who remained emmetropic (from Goss and Jackson, 1996).

2.3.2.2 Predicting progression of myopia

In 2011 Berntsen and colleagues reported a small but statistically significant increase in myopia progression with increased near exophoria. The progression was −0.004D per year for each prism dioptre of exophoria ($p = 0.046$). Goss and Rainey (1999) noted a relationship between higher esophoria and higher lag of accommodation in myopic children.

In summary, although many of these studies are not recent, atypical near phoria was consistently found to be a predictor of the onset and progression of myopia. Phoria that is close to normal values at near appears to be protective against myopic progression. There were no studies found that reported whether distance phoria measures are equally predictive.

2.3.3 Accommodative facility

2.3.3.1 Predicting progression of myopia

Allen and O'Leary (2006) noted that reduced accommodative facility was an independent predictor of myopic progression after following a group of 30 myopes and 34 non-myopes aged 18 to 22 years for 12 months.

2.3.3.2 Accommodative facility with myopia

The near accommodative facility has been shown to be the same for all refractive errors in young adults aged from 18 to 27 years (O'Leary and Allen, 2001) and children (mean age 6.7 ± 0.4 years) (Pandian *et al.,* 2006), with similar results reported by Jiang and White (1999). However, accommodative relaxation has been shown to take longer in myopes compared with emmetropes when viewing a near target in young adults (Jiang and White, 1999, Radhakrishnan *et al.,* 2007).

The distance accommodative facility is lower in myopes than emmetropes in young adults (O'Leary and Allen, 2001, Radhakrishnan *et al.,* 2007) and in a group of children with a mean age of 6.7 ± 0.4 years (Pandian *et al.,* 2006).

2.3.4 The accommodative convergence to accommodation (AC/A) ratio

2.3.4.1 Predicting onset of myopia

Jiang's 1995 study followed the refractive error changes of 44 college aged students. He found that AC/A ratios were higher in the six young adults who became myopic compared to those adults who remained emmetropic.

Similarly, Gwiazda and colleagues (2005) followed 80 emmetropic children aged six to 18 years, over three years. During this time 26 participants became myopic. They found a statistically significant elevation in the AC/A ratio one and two years prior to myopic development, at onset and then after onset of myopia compared to those children who remained emmetropic. AC/A ratio was measured using a Canon R−1 infrared open field autorefractor and was calculated as a response AC/A ratio.

Both lens induced and distance induced response AC/A ratios were found to be elevated in children with myopia compared to emmetropes (Gwiazda *et al.,* 1999). Lens induced AC/A ratios were significantly higher in myopic children compared to emmetropic children aged seven to 14 years (Sreenivasan *et al.,* 2009).

Zadnik and colleagues (2015) evaluated a subset of participants from the CLEERE study. A total of 414 children (average age on entry to the study 6.7 ± 0.5 years) who were emmetropic but became myopic through the course of their study were included. They identified 13 potential predictors including the binocular vision measures of AC/A ratio and accommodative lag. Univariate and multivariate analysis showed that an elevated AC/A ratio was a risk factor for the development of myopia.

2.3.4.2 Predicting progression of myopia

Jiang's (1995) study of 44 college aged students found that AC/A ratios were higher in seven of the 11 myopes who had progressing myopia compared to those adults who remained emmetropic. Similarly, a prospective study by Mutti and colleagues (2000) showed that those subjects with higher baseline AC/A ratios were at increased risk of myopic progression. In contrast, Chen and colleagues (2003) found no significant difference in the AC/A ratio of progressing myopes, stable myopes and emmetropes.

The AC/A ratio may be affected by near-vision work. Rosenfield and Gilmartin (1987) found after a 14 minute near-vision task the AC/A ratio was more elevated for early onset myopes (those who became myopic before they were 15 years old) compared to late onset myopes (those who became myopic after 15 years old) and emmetropes.

Price and colleagues (2013) reported that high AC/A ratios and lag of accommodation were significantly correlated to myopia progression. By improving accommodative lag, they found that there was a reduction in myopia progression in patients younger than 16.9 years. However, this effect was only noted in the first year.

In summary, there is not complete agreement between studies on the effect of accommodation and binocular vision functions on myopia onset and progression. However, some of these measures show more consistent associations than others. All studies reported high AC/A ratios to be a correlate of the onset of myopia. The AC/A ratios give an indication of the relationship between accommodation and vergence. Abnormalities in either function will lead to abnormal AC/A ratios. This may be why there are more consistent results with this test. Most studies published also confirm that AC/A ratios are correlated with myopia progression.

It is still unclear whether differences in binocular vision function are a trigger for myopic development or a result of changes in refraction. Altered accommodative facility was found to occur prior to myopia development (Allen and O'Leary, 2006) while, as just discussed, a similar longitudinal study by Mutti and colleagues (2006) found no association with lag of accommodation prior to myopia development. Studies to assess this association require the long-term follow-up of large numbers of children and may be influenced by the researcher's bias, correction options used, testing methods and frequency of testing.

It is postulated that the relative hyperopic blur with increased lag of accommodation at near is a stimulus for myopic development (Gwiazda *et al.,* 1993). In a review of myopia development, Wallman and Winawer (2004) note that there are several studies that have shown that accommodation is not necessary for eye growth but they go on to say that it cannot be excluded completely. In particular, prolonged periods of steady defocus (hyperopic defocus) that is associated with a lag of accommodation would seem likely to influence the eye's process of emmetropisation.

2.3.5 Changes to axial length with accommodation

Drexler and colleagues (1998) demonstrated that axial length increased with accommodation in adults. A greater change in axial length was found in emmetropes (0.013mm) compared to myopes (0.0052mm). They postulated that the change in axial length was due to the contraction of the ciliary muscle decreasing the circumference of the globe and increasing axial length.

Accommodation has been shown to transiently increase axial length in young myopic adults (mean age 21.5 ± 2.1 years) with accommodative demands of 2.00D, 4.00D and 6.00D after 20 seconds of viewing (Mallen *et al.,* 2006). Only early onset myopes were included in the study. Early onset was defined in this study as progression commencing before the age of 15 years. When presented with an accommodative demand of 6.00D, the axial length increase in myopes (mean 0.058mm or an approximate increase of 0.17D) was significantly greater than for emmetropes (mean increase 0.037mm or the equivalent of 0.10D, $p = 0.02$). The mean spherical equivalent refraction of the 'emmetropes' was −0.07 ± 0.23D (although this group included low myopes) and the myopes was −3.59 ± 0.75D.

A similar study of 40 adult subjects (mean age 25 ± 4 years) found axial length increased with accommodative demand of 3.00D and 6.00D, but did not find a difference between myopic (mean spherical equivalent refractive error −1.82 ± 0.84D) and 'emmetropic' eyes with mean spherical equivalent refractive error of −0.05 ± 0.27D. This study also included some low myopes in the 'emmetropic' group which may have influenced results. Measurements were taken as soon as the image was clear (Read *et al.,* 2010). This difference may be a result of the Read study having slightly older participants with less myopia and viewing the target for a shorter period compared to the Mallen study.

Woodman and colleagues (2011) investigated axial length following a slightly longer period of 30 minutes with sustained near work at 5.00D accommodative demand in adult emmetropes and myopes. Axial length increased in all participants. For analysis, myopes were categorized as early onset (defined as myopia that began before 12 years of age) or late onset. They were then sub-categorised in each group as stable or non-progressing. The early onset myopic and progressing myopic groups showed statistically significant increases in axial length compared to the emmetropes (early onset myopic 0.027 ± 0.021mm, progressing myopic 0.031 ± 0.022mm, and emmetropes 0.010 ± 0.015mm respectively). At the end of a 10-minute break from near work, axial length measures returned to baseline in all groups.

Summary of accommodation and binocular vision findings in relation to the onset and progression of myopia.

Lag of accommodation			
	Participants	**Summary findings**	**Testing method**
Predicting myopia onset			
Goss (1991)	150 children (6 to 15 years)	higher lag of accommodation in 'became myopic'	Fused cross cylinder
Drobe and deSaint-Andre (1995)	50 children (12.8±6.3 years)	higher lag of accommodation in 'became myopic'	Fused cross cylinder
Gwiazda *et al.,* (2005)	80 children (6 to 18 years)	increase lag of accommodation two years before myopia onset	Open field autorefractor
Mutti *et al.,* CLEERE (2006)	1107 children (6 to 15 years)	monocular lag of accommodation at 2.00D and 4.00D not different	Badal stimulus
Zadnik *et al.,* CLEERE (2015)	414 children (6.7±0.5 years)	not a risk factor for myopia onset with univariate and multivariate analysis.	Badal stimulus
With myopia			
Gwiazda *et al.,* (1993)	64 children (5 to 17 years)	myopes less accurate accommodation compared to emmetropes at near	Real target
Goss and Rainey (1999)	73 children (7.2 to 14.7 years)	myopes higher lag of accommodation and esophoria	
Wolffsohn *et al.,* (2003)	18 young adults	late onset myopes less accurate with 4.50D demand than early onset myopes or emmetropes.	
Nakatsuka *et al.,* (2005)	61 children (9.5±1.3 years)	fully corrected myopes larger lag of accommodation compared with emmetropes (lag of accommodation decreased with habitual correction)	Open field autorefractor
Mutti *et al.,* (2006)	568 children (6 to 15 years)	higher lag of accommodation after onset of myopia	Badal stimulus

Accommodation and binocular vision function and myopia (continued).

Lag of accommodation			
	Participants	**Summary findings**	**Testing method**
Predicting myopia progression			
Gwiazda (1995)	63 children (6 to 18 years)	higher lag of accommodation correlated with myopic progression	
Abbott *et al.,* (1998)	22 young adults	reduced accommodation response to minus lens-induced accommodative demand in progressing myopes compared to stable myopes. no difference in accommodation response in early onset myopes, late-onset myopes or emmetropes.	
Rosenfield et al., (2002)	23 young adults (23.0 years)	low lag of accommodation with 2.50D demand associated with increased myopic progression.	Open field autorefractor
Allen and O'Leary (2006)	young adults (18 to 22 years)	lag of accommodation independent predictor of myopic progression	
Price *et al.,* (2013)	142 young adults (14 to 21 years)	lag of accommodation and AC/A correlated with myopia progression. Improving lag of accommodation led to less myopia progression in the first year.	
Weizhong *et al.,* (2008)	62 children (10.8±1.6 years)	lag of accommodation no correlation with myopia progression.	Open field autorefractor
Berntsen *et al.,* (2011)	592 children (10.4±1.8 years)	lag of accommodation at baseline and after 1 year. Neither correlated with annual myopia progression	Badal stimulus

Accommodation and binocular vision function and myopia (continued).

Distance and near heterophoria		
	Participants	**Summary findings**
Predicting myopia onset		
Goss (1991)	150 children (6 to 15 years)	'became myopic' more eso posture compared to remained emmetropic group
Drobe and deSaint-Andre (1995)	50 children (12.8±6.3 years)	'became myopic' more eso posture compared to remained emmetropes
Goss and Jackson (1996)	87 children	near phoria not close to orthophoria risk factor for myopia development
With myopia		
Goss and Jackson (1996)	87 children	near phoria more eso posture with myopia
Goss and Rainey (1999)	73 children (7.2 to 14.7 years)	higher esophoria and higher lag of accommodation in myopes
Predicting myopia progression		
Berntsen *et al.*, (2011)	592 children (10.4±1.8 years)	very small increase in myopia progression with increased near exophoria

Accommodation and binocular vision function and myopia (continued).

Accommodative facility		
	Participants	**Summary findings**
With myopia		
Jiang and White (1999)	15-24 young adults	near accommodative facility the same for all refractive errors negative response time (relaxing accommodation) longer in myopes compared with emmetropes
Allen and O'Leary (2001)	79 young adults (18-27 years)	near accommodative facility the same for all refractive errors distance accommodative facility lower in myopes than emmetropes
Pandian *et al.,* (2006)	1328 children (6.7±0.4 years)	near accommodative facility the same for all refractive errors distance accommodative facility is lower in myopes than emmetropes
Radhakrishnan *et al.,* (2007)	20 young adults	negative response time (relaxing accommodation) longer in myopes compared with at near distance accommodative facility lower in myopes than emmetropes
Predicting myopia progression		
Allen and O'Leary (2006)	64 young adults (18 to 22 years)	accommodative facility independent predictor of myopic progression
Pandian *et al.,* (2006)	1328 children (6.7±0.4 years)	near accommodative facility the same for all refractive errors

Accommodation and binocular vision function and myopia (continued).

AC/A ratio		
	Participants	**Summary findings**
Predicting myopia onset		
Jiang (1995)	44 young adults	higher in young adults who became myopic and higher in most myopes with progressing myopia compared to those who remained emmetropic.
Gwiazda *et al.*, (2005)	80 children (6 to 18years)	higher AC/A ratio 1 and 2 years prior to myopic development, at onset, and after onset of myopia compared to those who remained emmetropic.
Zadnik (2015)	414 children (6.7±0.5 years)	AC/A a risk factor for myopia development univariate and multivariate analysis
With myopia		
Rosenfield and Gilmartin (1987)	81 young adults	short near-vision task AC/A ratio more elevated for early onset myopes compared to late onset myopes, and emmetropes
Gwiazda *et al.*, (1999).	101 children	AC/A ratio elevated with myopia compared to emmetropes
Gwiazda *et al.*, (2005)	80 children (6 to 18 years)	higher AC/A ratio 1 and 2 years prior to myopic development, at onset, and after onset of myopia compared to those who remained emmetropic
Sreenivasan *et al.*, (2009)	children (7 to 14 years)	AC/A ratio significantly higher in myopes compared to emmetropes
Predicting myopia progression		
Jiang (1995)	44 young adults	higher AC/A ratio in became myopic and most with progressing myopia compared to those who remained emmetropic
Mutti *et al.*, (2000)	828 children (6 to 14 years	higher baseline AC/A ratio at increased risk of myopia progression
Price *et al.*, (2013)	142 young adults (14 to 21 years)	AC/A and lag of accommodation correlated with myopia progression. Improving lag of accommodation led to less myopia progression in the first year
Chen *et al.*, (2003)	30 children (8 to 12 years)	no significant difference in the AC/A ratio of progressing myopes, stable myopes and emmetropes (East Asian)

Table 2-1 Summary of accommodation and binocular vision findings in relation to myopia and its onset and progression

2.4 Optical correction, binocular vision function and myopia control

2.4.1 Bifocal and progressive addition spectacle lenses

Bifocal and progressive spectacle lenses have been used as a method of myopia control for several decades. One of the first reported uses was by Warren (1955) who described using bifocals in an 18-year-old college student. It was suggested that wearing these lenses decreases the accommodative demand at near and thus reduces the stimulus for eye growth (Mandell, 1959).

Studies have shown that participants with baseline binocular vision function of near esophoria (Goss and Grosvenor, 1990, Fulk *et al.,* 2000, Hasebe *et al.,* 2008), increased lag of accommodation (Hasebe *et al.,* 2008, COMET 2, 2011) and a combination of esophoria at near and increased lag of accommodation (Gwiazda *et al.,* 2004, COMET 2, 2011) have a greater treatment effect. However, the treatment effect is small (Fulk *et al.,* 2000, COMET 2, 2011). This association has been demonstrated in Asian children (Brown *et al.* 2002, Yang *et al.,* 2009) which is significant as Asian children have been shown to have, on average, a more exophoric posture at near than Caucasian children (Leone *et al.,* 2010).

Berntsen and colleagues (2012) evaluated the impact of wearing progressive addition spectacle lenses in 85 myopic children (aged 6 to 11 years) with high accommodative lag and compared this to wearing single vision spectacles. Following lens wear for one year, there was a small but statistically significant decrease in myopia progression in the progressive addition lens group of −0.52D compared to −0.35D in single vision distance or a mean 30% reduction in progression. This study used short corridor progressive addition lenses of +2.00D add power.

Cheng and colleagues (2014) evaluated whether including prismatic correction in bifocal lenses improved the reduction in progression of myopia. One hundred and thirty-five myopic Chinese-Canadian children (mean age 10.29 years, range 8 to 13 years) were randomly assigned treatments of single vision distance, executive bifocals or executive bifocals with 3^{Δ} base in prism in each eye (prism bifocals). The near addition was +1.50D. Both bifocals and prism bifocals showed reduced myopic progression independent of initial near phoria. The mean reduction was 39% with bifocals and 51% with prism bifocals over three years. Children with high lag of accommodation had similar treatment effects with bifocals and prism bifocals, while those children with low lags had greater treatment effect with the prism bifocals. This study showed that the addition of base in prism in children with low lag of accommodation may be beneficial. The improved treatment effect with bifocal lenses may be due to the executive bifocal lens design which makes it easier to ensure that participants look through the near addition portion of the lenses for near work compared with progressive addition spectacles.

Figure Table 2-2 presents a summary of the effect of bifocal and progressive addition lens on myopia progression. These studies have all suffered from some limitations which will now be discussed. Wearing bifocal or progressive spectacle lenses may not be optimal as young myopes may not use the appropriate position of the lens for near tasks particularly while viewing computers. Not using the appropriate position may result in looking through the distance portion of the lenses and inducing the same accommodative demand as single vision spectacles. In addition, these studies had set near additions which were not tailored to individuals which could impact on the efficacy of the treatment. Bifocals may be less cosmetically accepted by children which could reduce compliance with wearing the lenses.

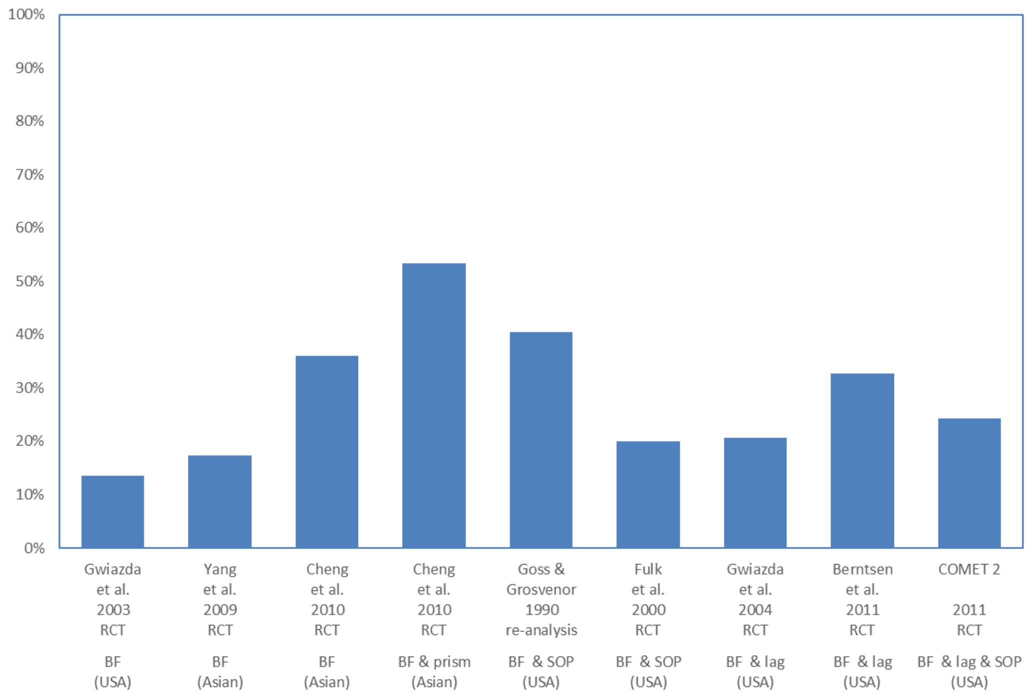

Figure Table 2-2 Comparison of reductions in myopia progression with bifocal or progressive addition spectacles from various studies. "RCT" indicates randomised controlled trial, "BF" indicates bifocal spectacles, "PAL" indicates progressive addition lens spectacles, "SOP" indicates esophoria at near and "lag" indicates lag of accommodation.

2.4.2 Bifocal soft contact lenses

There has been a growing use of bifocal soft contact lenses as a method of myopia progression control. The lag of accommodation has been found to be altered while wearing bifocal contact lenses compared to single vision contact lenses in myopes (Tarrant *et al.*, 2008) with a shift towards a lead of accommodation (myopic focus).

It should be noted that there is an alternative (non-accommodative) mechanism hypothesised for an effect of these lenses on myopia control via manipulation of relative peripheral defocus which is discussed further in section 2.6.1.

A case study involving a pair of twins who were randomly assigned to wear bifocal or single vision contact lenses showed that the child wearing bifocal contact lenses had smaller axial length growth and less refractive change than the child wearing single vision contact lenses. At baseline, both twins had esophoria at near (Aller and Wildsoet, 2008).

Aller and colleagues (2006, 2016) carried out a 12-month prospective, randomised controlled double masked clinical study comparing single vision contact lenses with bifocal contact lenses. They enrolled 86 myopes aged eight to 18 years with mean refractive error −2.69 ± 1.40D. They selected only subjects with eso fixation disparity at near measured with a Bernell Near Point Examination Card at 33cm. The power of the near addition was selected to minimize near fixation disparity. After 12 months of lens wear the axial length increased by 0.05 ± 0.14mm with bifocal soft contact lenses and 0.24 ± 0.17mm with single vision soft contact lenses. The difference between the two groups was statistically significant ($p < 0.001$).

Other studies using multifocal contact lenses have shown comparable results (Anstice and Phillips, 2011, Sankaridurg *et al.,* 2011, Walline *et al.,* 2013, Lam *et al.,* 2014). The treatment effects are typically larger than those found with bifocal or progressive spectacle lens wear. This may be due to more reliable use of the near addition portion of the contact lenses compared to spectacles. There are also variations in binocular vision function with bifocal contact lenses compared to spectacles which may have a myopia control effect (Tarrant *et al.,* 2008).

The type of bifocal contact lenses used in these studies were designed to provide a distance focus central portion of the lens and a near focus annulus surrounding the centre of the lens. This type of design matches the orthokeratology optical design which also has an area of distance correction with a steeper (more hyperopic) surrounding correction on the reshaped cornea. As bifocal contact lenses have been shown to alter binocular vision function (Tarrant *et al.,* 2008) and may have a treatment effect to reduce ocular axial length growth in subjects with esophoria, the effect may be similar in orthokeratology lens wear.

2.5 Accommodation and binocular vision function with orthokeratology lens wear

There is growing interest in investigating how accommodation and binocular vision status is affected by orthokeratology lens wear. McLeod and colleagues (2005) presented a poster at the American Academy of Optometry, the poster forming part of his Master's thesis (McLeod, 2006). Tarrant and colleagues presented a poster at the Association for Research in Vision and Ophthalmology Conference (2010). Brand (2013) published in Optometry and Visual Performance. More recently Felipe-Marquez and colleagues (2015, 2017) published two papers in Graefe's Archive of Clinical and Experimental Ophthalmology on the impact of orthokeratology lens wear on accommodation and binocular vision in young adults. Gifford and colleagues (2017) have compared near binocular vision function results of young adult orthokeratology lens wearers with age matched controls. These studies will now be reviewed in more detail.

McLeod (2005) evaluated phoria, vergence and accommodation in 29 children aged 8 to 14 years. Six subjects dropped out throughout the study although the data of these subjects were included. There were several limitations in this study including the small sample size and the choice of method of testing.

Subjective measurements of binocular vision included;

- Near lateral phoria using a modified Thorington test, using a phoropter and a testing distance of 40cm
- Fusional reserves (vergences) measured through a phoropter with a 20/30 letter size at 40cm

- Push up amplitude of accommodation measured through a trial frame using a 20/30 letter size on a near letter chart beginning testing at 40cm and moving closer toward the subject until blur was detected
- Lead or lag of accommodation using fused cross cylinder through the phoropter (the testing distance was not stated)
- Positive relative accommodation and negative relative accommodation through the phoropter using a 20/30 letter size on a near letter chart at 40cm.

Objective measurement of lead/lag of accommodation was determined using the Grand Seiko WR – 5100K Autorefractor (Japan). This has an open-view window for subjects to view real world targets. It is considered to be accurate and repeatable for both refractive and accommodative testing (Davies *et al.*, 2003). Five different distances were tested.

No significant difference was found in phoria measurements. Phoria measurements were compared in a "corrected" group, where residual refraction was corrected prior to measurement, and a second comparison was done as an "uncorrected" group, where initial uncorrected refractive error phorias were compared to uncorrected treatment phorias. It may have been better to compare habitual phoria while corrected with spectacles prior to orthokeratology lens wear to no residual refractive error correction during orthokeratology as this would be the habitual visual state of the subjects. Fusional vergences were also reported as unchanged but this may be due to the small sample size and the large variation in fusional vergence seen in the normal population.

No significant difference in binocular amplitude of accommodation was found. However, any accommodation above 18D was only recorded as 18D which may have skewed the results. The average level of accommodation found in this study was higher than expected. They referred to Hofstetter's (Borish, 1970) expected value of:

Amplitude of accommodation (D) = 18 – 1/3 age in years ± 2.00D

This was 13.3 to 14.7D based on the age of the subjects. This value is higher than a recent report from a study of six to 10-year olds in Sweden who had both a lower mean value of accommodation and greater variability of result of 12.4 ± 3.7D (Sterner *et al.,* 2004). The higher results seen in the McLeod study could be due to a poor choice of tests as the push up test is prone to overestimation of accommodation (Burns *et al.,* 2014). They suggested that in future a push down test or minus lens to blur may improve the accuracy of the readings. Other ways to improve their results could be to introduce a negative lens (thus increasing accommodative demand) or carry out monocular amplitude of accommodation tests. This would remove the increased accommodation seen with binocular viewing (vergence induced accommodation) and may have given a better comparison. They argue that they were looking for differences in readings but do not comment on the repeatability of their method to give an idea of its validity. A recent review highlights several limitations of widely used methods of measuring the amplitude of accommodation (Burns *et al.,* 2014).

Near accommodative facility was found to be no different after lens wear. The testing method they used may not have been sensitive enough to find the subtle differences that may have occurred. Previous studies that have found differences in accommodative facility with myopia compared to emmetropia have used more precise techniques, timing the rate of change in accommodation in the positive and negative directions (Jiang and White, 1999, Radhakrishnan *et al.,* 2007). They also did not test the distance accommodative facility which has been shown to be reduced with myopia (O'Leary and Allen, 2001, Radhakrishnan *et al.,* 2007) and could possibly alter more significantly with orthokeratology lens wear.

No significant change was reported in the lag/lead of accommodation when measured subjectively. It was only tested at one distance and through the phoropter. When measured objectively over five different distances with an open view auto-refractor, the gradient of the slope of accommodative lag decreased with orthokeratology lens wear meaning that the participants had more accurate accommodation over a range of focussing distances.

Tarrant and colleagues (2009) determined the lag of accommodation in 28 myopic subjects wearing soft contact lenses and then four weeks after fitting them with orthokeratology lenses. Ocular aberrations were measured with a COAS wavefront analyser (Abbott Medical Optics, USA) at five different focussing distances. Although not clear in this publication the authors have published elsewhere a method of determining accommodation from these measurements (Tarrant *et al.,* 2010). They found that at all distances the lag of accommodation was reduced while wearing orthokeratology lenses compared to soft contact lens wear. They conclude that this effect could explain how orthokeratology lens wear slows myopic progression.

Brand (2013) reviewed the records of 11 patients seen in a private optometric practice. The age range was large in this group ranging from 11.0 to 36.8 years with a mean age of 18.4 ± 9.6 years. He noted that as a group there was a statistically significant increase in mean accommodative facility, and a decrease in mean lag of accommodation and gradient AC/A ratios. These findings represent improved (normalised) functions. Although there was a slight shift in near phoria in the exo direction it failed to reach statistical significance ($p = 0.09$).

In addition to analysing the data from the whole cohort, he assessed the individual patient's accommodation and binocular vision profiles prior to lens wear and during lens wear. From this analysis, he noted an improvement in accommodation and binocular vision profile in 10 of the 11 patients, while one patient's profile remained unchanged. He concluded that orthokeratology lens wear could improve the accommodative convergence function. This study was limited by the small sample size and large range of age of patients investigated, and potential investigator bias with categorising individual accommodation and binocular vision status and when testing.

Felipe-Marquez and colleagues (2015) reported on changes to accommodation with short and long-term wear of orthokeratology lenses, with a follow-up report on binocular vision changes in the same cohort (Felipe-Marquez *et al.,* 2017). Participants were young adults (age range 18 to 30 years) who were randomly selected to a control group, a Paragon CRT lens (Paragon Vision Sciences; Interlenco, Madrid, Spain) group and a Seefree lens (Conoptica, Barcelona, Spain) group. Participants were followed for three months. A separate group of long term Paragon CRT lens wearers were used for a three-year follow-up group.

Mean monocular amplitude of accommodation (minus lens method), near monocular accommodative facility with ±2.00D flipper lenses at 40cm for one minute, positive and negative relative accommodation and lag of accommodation measured with monocular estimate method were unchanged in the control and both lens groups in the short term. When comparing the three-month data with an age matched group of orthokeratology lens wearers who had worn lenses for three years, negative relative accommodation improved with long term wear ($p = 0.0006$) (Felipe-Marquez *et al.,* 2015).

In a follow-up publication, (Felipe-Marquez *et al.,* 2017) binocular vision function is reported. The report appears to have used the same participants as their earlier study (Felipe-Marquez *et al.,* 2015). There was no change in mean distance phoria measured with the Von Graefe method, gradient AC/A ratio using Von Graefe phoria with −1.00D lenses, or near point of convergence. Mean near phoria shifted in the exo direction in the orthokeratology lens group in the short-term group (baseline mean $-2.5 \pm 4.3^{\Delta}$ to three months mean $-3.8 \pm 3.8^{\Delta}$; $p = 0.005$). In the longer term, the distance base out recovery point increased ($19.7 \pm 6.2^{\Delta}$ to $24.6 \pm 9.6^{\Delta}$; $p = 0.02$). Although not discussed in the paper, there appeared to be an increase in the range of distance phoria with long term lens wear indicated by the large difference in standard deviations reported ($0.2 \pm 0.3^{\Delta}$ at three months compared to $-0.4 \pm 1.5^{\Delta}$ at three years).

It is interesting that different lens wearing groups had different results. This may be due to the different optical effects of the lenses due to different treatment sizes or power of reverse curves, or may be due to differences in baseline accommodative and binocular vision function.

Gifford and colleagues (2017) reviewed the records of patients seen in private practice. Accommodation and binocular vision function of 17 young adults (aged 18 to 30 years, mean age 25.8 ± 3.2 years) wearing orthokeratology lenses were compared with soft contact lens wearers matched for age, level of refractive error and duration of lens wear. Horizontal phoria, positive and negative fusional reserves and lag of accommodation were measured at near.

The orthokeratology group had statistically significantly more exophoria at near (mean $-2.05 \pm 2.38^{\Delta}$) compared to soft contact lens wearers ($0.00 \pm 1.46^{\Delta}$) ($p = 0.005$). The orthokeratology lens wearers also had lower lag of accommodation (mean +0.97 ± 0.33D) compared to soft contact lens wearers (mean +1.28 ± 0.32D) ($p = 0.009$). Lag of accommodation was determined using the monocular estimate method retinoscopy. Fusional reserves were not statistically different in the two groups.

This study was limited by using aged matched controls which may not have controlled for time since onset of myopia, which could influence binocular vision results. In addition, soft contact lens wear has been shown to alter accommodation and binocular vision function compared to spectacle lens wear (Jimenez *et al.,* 2011). The method used for testing lag has been shown to be less repeatable than other methods (Antona *et al.,* 2009) and may be less reliable in orthokeratology lens wear due to the altered corneal shape. There may also have been investigator bias in measuring accommodation and binocular vision tests as the monocular estimates method is an objective test.

There is agreement between studies on the impact of orthokeratology lens wear on distance phoria (no change) and near fusional reserves. The two studies that compared lag of accommodation to soft contact lens wear both found a decreased lag. The same result was not found when lag was compared to baseline measures with spectacles. Two studies found a shift in the exo direction with near phoria, while two studies did not. This difference may be due to the different testing methods used for near phoria or the type of optical correction used for baseline measurements.

A summary of the findings from these studies is presented in Table 2-3.

	McLeod 2005	**Tarrant *et al.* 2009**	**Brand 2013**	**Felipe-Marquez *et al.* 2015, 2017**	**Gifford *et al.* 2016****
n	29	28	11	25	17
Age (years)	8 to 14	Young adult	11 to 37	18 to 30	18 to 30
Distance phoria	x	x	NSC	NSC	x
Near phoria	NSC	x	more exo (p=0.1)	NSC	more exo
Lag of accommodation	NSC	decrease	NSC	NSC	decrease
Negative relative accommodation	NSC	x	x	increase (long term)	x
Positive relative accommodation	NSC	x	x	NSC	x
AC/A ratio	x	x	decrease (AC/A −1)	x	x
Accommodative facility	NSC	x	increase	NSC near monocular	x
Spherical aberration	x	increase	x	x	x
Near fusional reserves		x	NSC	x	NSC

Table 2-3 Summary of findings from studies investigating accommodation and binocular vision in orthokeratology lens wear. "x" indicates outcome variable not included in the report. ** Study compared orthokeratology lens wearers to soft contact lens wearers. "NSC" indicates no significant change.

2.6 Orthokeratology as a form of myopia control

The first published article on the possible myopia control effect of orthokeratology was a retrospective review by three optometric practitioners in private practice (Reim *et al.,* 2003). They reviewed the records of 462 consecutive eyes fit with orthokeratology lenses. Only patients under 18 years old were analysed. Data were available for 294 eyes seen at a three-month visit (used as a 'baseline'), 12-month data for 253 eyes and three-year data for 164 eyes. The outcome measure they used for analysis was subjective over-refraction (the residual refractive error after orthokeratology treatment). This approach has several limitations including the poor level of repeatability and reliability of subjective refraction (Bullimore *et al.,* 1998), the variability of the orthokeratology effect on a daily basis and its variability throughout the day (Swarbrick, 2006). They determined an average rate of progression of myopia of 0.13D per year which they concluded was similar to wearing conventional rigid gas permeable contact lenses. They quoted several other papers which reported average levels of myopic progression but these were not matched for age, ethnicity or initial refractive error and time since diagnosis which could influence the result. They acknowledged the many limitations of doing a retrospective review and the methods used, but they argued that positive results would help instigate more costly and time consuming prospective studies.

Two prospective studies using a historic control have been completed and reported in the literature (Cho *et al.,* 2005, Walline *et al.,* 2009). The outcome measurement for myopia progression used in both studies was change in ocular axial length. Axial length measurements are objective and thus less prone to researcher bias. Cross sectional and longitudinal studies have shown a strong relationship ($R = 0.83$, $p < 0.005$, Hosaka, 1988, coefficient of determination (R^2) = 0.53, $p < 0.001$, Atchison *et al.,* 2004) between axial length growth and myopic progression, although there is individual variation. Axial length is related to change in refractive error although other ocular components may alter to maintain emmetropisation. An approximation for the change in refractive error with axial length change and no compensation of other ocular components is that 1.0mm change in axial length is equivalent to 3.00D refractive error change (Carroll, 1981, Grosvenor and Scott, 1991, Chau *et al.,* 2004, Atchison *et al.,* 2004).

The first paper published was by Cho, Cheung and Edwards (2005). Measurements of variables of interest were carried out by the researchers whereas optometric care was carried out by private practitioners. There was no standard protocol for the fitting of the lenses. Forty-three subjects aged seven to 12 years were enrolled and 35 completed the two-year study period. This represents a drop-out rate of 19% which is similar to other prospective orthokeratology studies carried out on adults that had drop-out rates of 23% (Tahhan *et al.,* 2003, Sorbara *et al.,* 2005). Four drop outs were due to an adverse response to orthokeratology lenses which included corneal fluorescein staining or corneal infiltrates. Other drop outs were due to lens damage, moving away from the study location in Hong Kong, and concern over reports of orthokeratology safety. Those who completed the study were matched for age, gender and baseline spherical equivalent refractive error with a control group from a previous study of single vision spectacle lens wearers conducted at the same institution (Edwards *et al.,* 2002). The data were presented for the right eye only as the left showed similar results.

One of the main outcome indicators was axial length. It was measured using A-scan ultrasonography. To eliminate inter-observer variability the same observer and measurement technique were used at baseline and throughout the study in both the orthokeratology lens wear and the historical control groups. The mean axial length of orthokeratology lens wearers increased by 0.29 ± 0.27mm compared to 0.54 ± 0.27mm in the spectacle lens wearing group. This was a statistically significant difference between the two groups ($p < 0.001$).

In the USA, Walline and colleagues (2009) used a similar approach to Cho, Cheung and Edwards (2005). Their study was funded by four contact lens industry companies. The authors noted that their industry supporters were not involved in any decision making throughout the study.

Forty subjects aged eight to 11 years were enrolled and 28 subjects completed the two-year study period. They were all fitted with the same orthokeratology lens design. There was a drop-out rate of 30%. This was slightly higher than the study by Cho and colleagues (2005). They attributed the drop-outs to lack of interest in contact lens wear. They did compare group baseline data of the drop-outs to those who carried on with the study and found no statistically significant difference between them. Only those who completed the study were used in the statistical analysis.

This study also used A-scan ultrasonography to measure axial length but measurements were made under cycloplegia. They compared the results to a group of soft contact lens wearers enrolled in a previous study conducted by the same research centre (The CLAMP Study, Walline *et al.*, 2004). The difference in change in mean axial length between the two groups was 0.22 ± 1.12mm over the two-year period. Again, this difference was found to be statistically significant ($p = 0.0004$). The large standard deviation found in this study also highlights the large individual variation in response to myopia progression control treatment.

The use of controls enrolled in a previous study rather than by random allocation by both the studies reduces their validity. This approach could introduce bias as the researchers had some level of control over who was included. Both authors recognised the limitation of this study design and recommended that prospective randomised controlled trials were warranted to help improve the quality of evidence.

However, some notable points are the choice of method used to measure axial length and the individual variability of response to orthokeratology lens wear.

Five of the studies (Cho and Cheung, 2010, Kakita *et al.,* 2010, Hiraoka *et al.,* 2012, Santodomingo-Rubido *et al.,* 2013, Swarbrick *et al.,* 2015) have shown a slower rate of axial length progression with orthokeratology lens wear compared to control eyes wearing contact lenses or spectacles. These studies used partial coherence interferometry (IOLMaster Zeiss, Germany) to measure the axial length.

Table 2-4

Study	**Length** (years)	**Location**	**Study design**	**Axial length measurement technique**	**Treatment/ Control**	**n**	**Age** (years ± SD)	**Change in axial length** (mm ± SD)
LORIC **Cho *et al.* 2005**	2	Hong Kong	Prospective historical control	A-scan ultrasound	OK	35	9.6 ± 1.5	0.29 ± 0.27
					Spectacles	35	9.6 ± 0.7	0.54 ± 0.27
Walline *et al.* 2009	2	USA	Prospective historical control	A-scan ultrasound	OK	28	10.5±1.1	0.22 ± 1.12*
					Soft CL	28	10.5±1.0	
SMART **Eiden 2010,** **Davis *et al.* 2015**	2-3	USA	Prospective randomised control	A-scan ultrasound	OK	**	8–14	R=0.00 L=0.10
					SH CL		8–14	R=0.00 L=0.30
MCOS **Santodomingo-Rubido *et al.* 2013**	2	Spain	Prospective randomised control	PCI	OK	31	6–12	0.47
					Spectacles	30	6–12	0.69
ROMIO **Cho & Cheung 2012**	2	Hong Kong	Prospective randomised control	PCI	OK	37	6–10	0.36 ± 0.24
					Spectacles	41	6–12	0.63 ± 0.26
Hiraoka *et al.* 2012	5	Japan	Prospective	PCI	OK	22	10.0±1.4	0.99 ± 0.47
					Spectacles	21	10.0±1.6	1.41±0.68
Swarbrick *et al.* 2015	0.5	Australia	Prospective cross over	PCI	OK	26	10.8–17.0	1st 6 mths −0.02±0.05 2nd 6 mths−0.04±0.08
					RGP CL	26	10.8–17.0	1st 6 mths 0.04±0.06 2nd 6 mths 0.09±0.09

Summary of orthokeratology myopia control studies. * Walline study results are the difference in axial length between the two groups at the end of the study. **The number of participants not reported. "n" indicates the number of subjects. "SD" indicates standard deviation. "PCI" indicates partial coherence interferometry.

The SMART study (Eiden *et al.,* 2009, Nixon, 2010, Davis *et al.,* 2015) did not show a significant change in axial length. They used A-scan ultrasound which has been shown to have a repeatability one order of magnitude less than the IOLMaster (Zeiss, Germany) (Santodomingo-Rubido *et al.,* 2002) which may account for the difference. This study was also being carried out by multiple practitioners in multiple practices which introduced inter-observer variability. In their interim results, they have found a statistically significant difference in refractive error between the two groups. However, as previously discussed, using refractive error as an outcome measure has several limitations (Bullimore *et al.,* 1998).

A report of the SMART study results following 3 years of treatment (Davis *et al.,* 2015) also found no difference in axial length with orthokeratology lens wear compared to control. Again they noted a statistically significant difference in refractive error in the two groups, with orthokeratology lens wearers exhibiting less refractive error change (−0.13 ± 0.62D) compared to the control group (−1.03 ± 0.58D). The SMART study was originally designed as an ongoing five-year study with other outcome measures being studied including safety of lens wear, but the study was not completed.

Hiraoka and colleagues (2012) reported that the myopia progression control treatment in orthokeratology lens wear was most effective in the first three years of treatment, with axial length increasing at similar amounts to myopic children wearing spectacles following this time. This may be a result of reduced effect of orthokeratology with time, or a reflection of the children showing slower axial length growth with increasing age.

Partial correction of myopic refraction with orthokeratology lens wear may also control myopia progression. In a study in Hong Kong (Charm and Cho, 2013), 52 young myopes (aged 8 to 11 years) were randomly allocated to being fitted with orthokeratology lenses that partially corrected their myopia or single vision distance spectacles. For the orthokeratology lens wearers, an orthokeratology correction target of

−4.00D was used and the residual refraction was corrected with single vision spectacles. After 1 month, only 19 participants continued in each group and analysis was completed on these participants only. Mean axial length change after 24 months was 63% lower in the orthokeratology lens wear group compared to the spectacle wearing control group. However, the drop-out rate in this study was high with 37% (7 from 19) in the orthokeratology lens wearing group and 16% (3 from 19) in the spectacle lens wearing group failing to complete the 5-year study. The authors attribute the high drop-out rate due to the number of follow-up visits required.

Many myopic children also have a significant astigmatic component to their refractive error. Astigmatism can be corrected by toric orthokeratology lenses. Correction with toric orthokeratology lenses was reported to reduce axial length growth by 52% over a two-year period compared to spectacle lens wear (Chen *et al.,* 2013). The 80 young participants in this study were not randomly allocated into the spectacle lens or toric orthokeratology lens wear groups which may have influenced results.

More recently meta-analyses of myopia progression control treatment efficacy have been reported (Si *et al.,* 2015, Sun *et al.,* 2015, Huang *et al.,* 2016). Si and colleagues (2015) report an overall myopia progression treatment effect of orthokeratology lens wear of -0.26mm per year (95% confidence interval 0.31 to 0.21mm, $p < 0.001$). Sun and colleagues (2015) report an overall treatment effect of 0.27 mm (95% confidence interval 0.22 to 0.32) less than the control group. They equate this reduction in progression to approximately 45%. They also note that the effect is similar in Asian and non-Asian populations, although they do qualify this with saying that the sample for non-Asian populations is small. Similarly, Huang and colleagues (2016) reported that orthokeratology exerts a moderate myopia progression treatment effect with an average axial length growth of −0.15mm per year (95% confidence interval −0.22 to −0.08). Their meta-analysis also included other myopia progression treatments. In comparison the myopia progression control treatment effect with orthokeratology was slightly better than the effect of dual focus (bifocal) contact lenses (−0.11mm per year, 95% confidence interval −0.25 to −0.05) and similar to low dose atropine (−0.15mm per year, 95% confidence interval −0.25 to −0.05).

The results from all these studies have strengthened the evidence for orthokeratology lenses controlling myopic progression in some individuals. There is consistency of the results with all studies showing either a slowing of axial length growth or a slowing in the progression of refraction. The results are not only statistically significant but they are also clinically relevant. The studies have been carried out in several locations around the world, including Australia, Hong Kong, Spain, Japan and the USA, suggesting a generalisability of results to different ethnicities, lifestyles and age groups.

Cho and colleagues (2005, p79) noted in their paper that: "*there are substantial variations in the degree of eye elongation among children and there is currently no way to predict the degree of slowing for any individual.*" There is still a need to understand the underlying mechanisms of myopia control with orthokeratology lenses to better predict its efficacy and to tailor treatment to individuals. Cho and colleagues (2005) postulated that as higher-order optical aberrations were altered by orthokeratology lens wear (Joslin *et al.* 2003 *p78*), these changes may *"trigger mechanism(s) leading to a slowing of eye growth".* Walline (2007) speculated that the force of the orthokeratology lens could exert pressure on the eye such that it grew more equatorially and less axially. This idea has, to the best of my knowledge, not been followed up with further research. As an alternate theory, he noted that orthokeratology lenses may provide an image shell in the periphery that "*may act as a signal for slowed eye growth*". Walline and colleagues (2009) noted that the effect of orthokeratology lenses on the peripheral refraction was the leading theory to explain the myopic progression control seen in orthokeratology lens wear. As this last hypothesis is still favoured amongst orthokeratology myopia control researchers it will be discussed briefly below.

2.6.1 Peripheral refraction

Animal studies have shown a greater role of the peripheral retina in refractive error development than previously thought. Wallman and colleagues (1987) found localised retinal areas of myopia development when localised areas of the retina are subject to form deprivation in chicks. Similarly, the choroid thinned with form deprivation in a localised fashion (Wallman *et al.,* 1995, cited in Nickla and Wallman, 2010). In the primate eye the peripheral retina has been found to contribute significantly to the emmetropisation process (2004, Smith III *et al.,* 2005, Smith III *et al.,* 2007, Hung *et al.,* 2008). Relative peripheral myopia was found to inhibit myopic progression in infant monkeys in a study by Smith III and colleagues (2009). Benavente-Perez and colleagues (2012) also reported that the relative peripheral myopic refraction inhibited myopia progression in Marmosets. This effect was not seen in chick eyes in one study (Schippert, 2006) but 2-zone contact lenses which induced relative peripheral myopia were found to alter refractive growth in chicks (Liu *et al.,* 2011).

Myopic eyes have been shown to have an altered shape (Deller, 1947, Mutti *et al.,* 2000, Atchison *et al.,* 2004, Gilmartin *et al.,* 2013) and hyperopic peripheral refraction (Hoogerheide *et al.,* 1971, Millodot, 1981, Mutti *et al.,* 2000, Seidemann *et al.,* 2002, Atchison *et al.,* 2006). In humans, the peripheral refraction has been shown to alter prior to the onset of myopia and continues to alter throughout myopic development (Mutti *et al.,* 2007). In addition, conventional myopic correction with spectacles (Lin *et al.,* 2010) or soft contact lenses (Kang *et al.,* 2012) has been shown to induce a relatively hyperopic refraction which is thought to stimulate eye growth.

The peripheral refraction profile of the eye has been shown to change with orthokeratology lens wear (Charman *et al.,* 2006, Kang and Swarbrick, 2016) with a more myopic refraction in the periphery relative to the central refraction. It is speculated that this change in refraction profile better matches the shape of the myopic eye and myopic defocus in the periphery may signal to the eye to discontinue growth (Figure 2-3 and Figure 2-4).

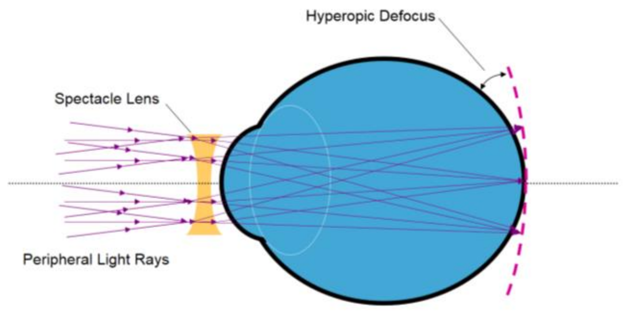

Figure 2-3 Myopic eye corrected with spectacle lenses (image courtesy of Dr Edward Lum, UNSW).

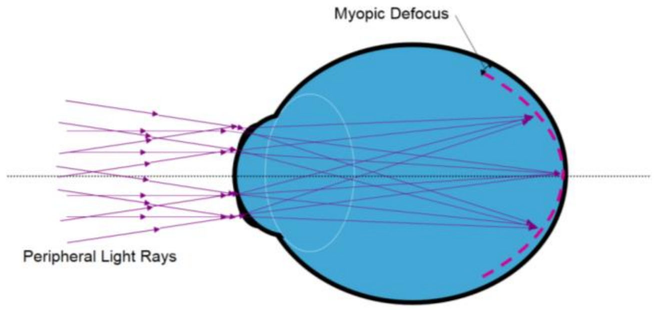

Figure 2-4 Myopic eye corrected with orthokeratology or multifocal soft contact lenses (image courtesy of Dr Edward Lum, UNSW).

However, Stone and Flitcroft (2004) in their review of ocular shape and myopia, note that eye shape varies both between and within refractive error groups suggesting that there may be different distinctive mechanisms that cause myopia to develop. They suggest that previous studies on myopia development may be confounded by grouping together these distinct growth mechanisms and suggest further myopia control research should use eye shape as a classification. This implies that eye shape and peripheral refraction may only be one of many possible mechanisms for eye growth.

Further, Mutti (2011) retrospectively analysed data from a large longitudinal study on myopia development. He noted that relative peripheral myopia (as seen in orthokeratology lens wear) appeared to have little consistent influence on the risk of the onset of myopic refractive error, the rate of myopic progression and axial length elongation.

Atchison and colleagues (2015) also noted that the relative peripheral refraction did not predict either the development or progression of myopia in a large cohort of Asian children (1,700 children aged 7 years at baseline and over 1,000 children aged 14 years at baseline). The children were followed for one and two years for the seven-year-old group and one year for the 14-year-old group. Both groups had myopia progression that was not associated with peripheral refraction using simple linear regression models. In addition, those who went on to develop myopia did not have more initial relative peripheral hyperopia than those who remained emmetropic suggesting an alternative mechanism for the onset of myopia.

2.7 Conclusions of literature review

It is clear from this review that myopia onset and progression is multifactorial and cannot be fully explained by peripheral refraction or by accommodation and binocular vision alone. The very large inter-individual variation also suggests that different factors may interact in different ways in individuals. Some of these differences may be difficult to determine in large trials particularly when there is emphasis placed on mean results.

While the evidence is equivocal, accommodation and binocular vision function may play a role in the onset and progression of myopia in some individuals. Maintaining clear vision through improving accommodation and binocular vision with optical correction has been found to have an effect on myopia progression control even though this effect may be small (Walline *et al.,* 2011). There is growing interest in the impact of orthokeratology on binocular vision function with most studies showing some changes with lens wear.

There is evidence that orthokeratology lens wear can slow myopia progression. Orthokeratology lens wear has been shown to alter the peripheral retinal focus. It is possible that these changes may alter accommodation and binocular vision function. The possible role of the accommodation and binocular vision function changes associated with orthokeratology lens wear has not been investigated.

2.8 Rationale and structure of thesis

There is a growing body of evidence that the use of orthokeratology lenses slows myopia progression in some individuals. One of the most commonly accepted hypotheses as to how orthokeratology lenses could do this is by altering the peripheral image shell to better match the myopic eye shape and produce peripheral myopic defocus. An image shell with myopic defocus may impact on accommodation and binocular vision function. However as myopic development may be multi-factorial, an alternative hypothesis including the role of accommodation and binocular vision function is worthy of investigation.

For example, myopes have been shown to have a greater lag of accommodation at near than emmetropes and this lag of accommodation may be a stimulus for myopic eye growth. It is unclear whether this difference in accommodative response is a trigger for myopic development or a result of changes in refraction associated with myopia development. Two studies (Tarrant *et al.,* 2010, Gifford *et al.,* 2016) have found that the lag of accommodation is altered in orthokeratology lens wear. This effect could be further evaluated.

The research questions that will be addressed in this thesis are:

1 Does accommodation and binocular vision function prior to myopia progression control interventions have any association with the efficacy of treatment?

No evidence could be found in the literature addressing this question. As other forms of optical treatment are influenced by the baseline accommodation and binocular vision, it is possible that there may be a similar effect with orthokeratology lens wear. The influence of accommodation and binocular vision function on the myopia progression during myopia control treatments also warrants further investigation.

2 How does myopia progression control treatments impact accommodation and binocular vision?

There is limited evidence available on how accommodation and binocular vision function responds to orthokeratology lens wear and this area warrants further investigation. Changes in accommodation and binocular vision could alter image quality and influence myopia development.

If certain binocular vision functions are associated with greater treatment effects, treatments could be better tailored to individuals.

3 Methods

This chapter is a review of the methods used in this thesis. The thesis is comprised of 4 studies addressing the 2 key research questions.

In this thesis two studies investigate possible associations between baseline accommodation and binocular vision function and the efficacy of myopia progression control treatments:

- Study 1: Review and re-analysis of data from a previously completed randomised controlled trial of orthokeratology lens wear
- Study 4: A retrospective review of clinical records of children seen in a university optometric clinic.

Three studies investigate the impact of orthokeratology on accommodation and binocular vision function:

- Study 2: A retrospective review of clinical records of myopic children and young adults seen in 2 private practices
- Study 3: A short-term prospective study of myopic young adults
- Study 4: A retrospective review of clinical records of children seen in a university optometric clinic.

In addition, the final study (Study 4) investigated the impact of low dose atropine on accommodation and binocular vision function.

3.1 The impact of baseline accommodation and binocular vision on the efficacy of myopia progression control treatments

Two studies are aimed at investigating whether baseline accommodation and binocular vision influence the efficacy of myopia control treatments. The first study (Study 1, Chapter 4) is a secondary analysis of the data obtained from a previously completed prospective study. I was involved in the development and implementation of the original study and am a co-author (under the name Watt, K.) of the published results (Swarbrick *et al.,* 2015). Accommodation and binocular vision of participants was determined at the commencement of the study as part of their routine optometric care. The data presented in this thesis have not been previously analysed or reported. Results from the secondary analysis led to the development of this thesis, including investigating how accommodation and binocular vision may be altered with myopia progression control treatment. The final study (Study 4, Chapter 7) is a retrospective analysis of clinical data of orthokeratology lens wearing children and children treated with low dose atropine in a Myopia Control Clinic at UNSW to investigate whether baseline accommodation and binocular vision status influences efficacy of treatment.

3.2 The impact of myopia progression control methods on accommodation and binocular vision

Three studies reported in this thesis are aimed to assess the impact of myopia progression control methods on accommodation and binocular vision. The first study to investigate this question was Study 2 (Chapter 5). It is a retrospective analysis of clinical data of orthokeratology lens wearing patients from two optometric practices in Australia. Results from this analysis were used to develop subsequent studies. Study 2 is followed up by a prospective short-term (1 month) study (Study 3, Chapter 6) of young adults on the effect of orthokeratology lens wear. The final study (Study 4, Chapter 7) is a retrospective analysis of clinical data of orthokeratology lens wearing children and children treated with low dose atropine in a Myopia Control Clinic at UNSW.

Details of the methods used, including the rationale for the tests used and the study design and statistical analysis can be found in each chapter.

Impact of baseline accommodation and binocular vision on efficacy of treatment						
Study	**Research method**	**Ethnicity**	**Method of myopia control**	**n**	**Age years**	**Duration**
1	Secondary analysis of prospective randomised control trial	South East Asian	Orthokeratology	26	10.5 to 16.6	6 months
4	Retrospective analysis	Mixed	Orthokeratology	9	9.5 to 14.8	Approx 6 months
			Low dose atropine	18	6 to 14	Approx 6 months
Accommodation and binocular vision with myopia progression control treatment						
Study	**Research method**	**Ethnicity**	**Method of myopia control**	**n**	**Age years**	**Duration**
2	Retrospective analysis	Mixed	Orthokeratology	37	8 to 20	Up to 1 year
3	Prospective study	Mixed	Orthokeratology	15	18 to 38	1 month
4	Retrospective analysis	Mixed	Orthokeratology	9	9.5 to 14.8	Approx 6 months
			Low dose atropine	18	6 to 14	Approx 6 months

Table 3-1 Summary of participants in each of the studies of this thesis.

3.3 Binocular vision status and accommodation

A detailed review of the common tests used to measure binocular vision and accommodation clinically and in the studies of this thesis can be found in Appendix C (p. 215). The individual tests are grouped under the heading of the specific accommodation or binocular vision function they are designed to assess. The rationale behind each accommodation and binocular vision function test is discussed followed by a brief description of the method of performing the test. The mean values and repeatability of tests are included where possible for adult and child populations. The limitations of the tests are also discussed.

Testing of binocular vision and accommodation can be broadly categorised into those tests that alter the stimulus to vergence (heterophoria and fusional reserves), tests that alter the stimulus to focussing or accommodation (accuracy of accommodation and positive and negative relative accommodation) and those that alter both (amplitude of accommodation, gradient AC/A ratio). Although this distinction has limits due to the strong association between the vergence and accommodation systems the tests will be presented in this order.

In 1944 Morgan published a set of normative values and standard deviations for a range of binocular vision tests carried out on young adults. A table adapted from these results can be found in Appendix D (p. 235). The results were taken from several papers and combined. They are still used in current clinical practice (Evans, 2007, Scheiman and Wick, 2014).

Methods used to measure accommodation and binocular vision used in this thesis include tests of phoria (von Graefe, Howell Phora Chart), fixation disparity (Saladin Card, Sheedy Disparometer), fusional reserves, accuracy of the accommodative response (Cross cylinder technique, monocular estimate method retinoscopy), positive and negative relative accommodation, accommodative facility, amplitude of accommodation and stereopsis (Titmus).

3.4 Ocular biometry

3.4.1 Axial length

The axial length of the eye has been measured with various techniques including X-ray (Deller 1947), magnetic resonance imaging (MRI) in both 2 dimensions (Atchison *et. al.,* 2004) and in 3-dimensions (Gilmartin *et. al.,* 2013), and with partial coherence interferometry. Throughout this thesis, axial length was measured using partial coherence interferometry using the IOL Master (Zeiss, Germany).

3.4.1.1 IOLMaster (Zeiss, Germany)

The Zeiss IOLMaster is an optical biometry instrument which uses partial coherence interferometry to measure the axial length of the eye. It was designed to be used to determine ocular biometry prior to intra-ocular lens (IOL) surgery. Measurements are taken from the anterior surface of the corneal epithelium to the retinal pigment epithelium. The test is non-invasive. It has been shown to have good repeatability and accuracy in adults (Lam *et al.,* 2001) and children (Carkeet *et al.,* 2004). In addition, the IOLMaster measures corneal curvature and anterior chamber depth. The anterior chamber depth measurements have been found to be less accurate than other methods (Lam *et al.,* 2001) and were not used in any of the analysis in the studies in this thesis.

Axial length has been found increase with accommodation (Drexler *et. al.,* 1998, Mallen *et. al.,* 2006, Read *et. al.,* 2010 and Woodman *et. al.,* 2011). It also varies throughout the day (Chakraborty *et al.,* (2011). To minimise variation measurements are made at a similar time of day and not following high accommodative demands.

Patients view a small red target and patients are aligned. Multiple readings are taken with a maximum of 20 readings per eye per day. For analysis 5 readings within 10µm were averaged.

Axial length was used as a proxy for myopic progression as orthokeratology lens wear alters the corneal shape in such a way that the underlying refraction cannot be determined.

3.4.2 Objective refraction

3.4.2.1 Shin-Nippon NVision-K 5001

The Shin-Nippon NVision-K 5001 (Tokyo, Japan) is an open field auto-refractor that uses infrared light to measure refractive error. Studies have reported similar results to non-cycloplegic subjective refraction in young adults (mean difference 0.14 ± 0.35 D p = 0.67) over a wide range of prescriptions (−8.25 to +7.25 D) (Davies *et al.,* 2003).

Patients are asked to view a distant target straight ahead through the open field viewer. A minimum of 5 readings are taken and an average is taken of these readings.

4 Review and re-analysis of data from a randomised controlled trial

This chapter (Study 1) is a review and re-analysis of data from a completed randomised controlled trial on orthokeratology and myopia progression to investigate any possible associations between baseline accommodative and binocular vision functions and changes in measurements of axial length and auto-refraction during treatment.

4.1 Background

This study aims to review and re-analyse the results of a previous study that investigated the effects of orthokeratology lens wear on myopia progression (Swarbrick *et al.,* 2015). The previous study was carried out by the Research in Orthokeratology (ROK) Group at UNSW between 2007 and 2010. I was a Research Optometrist working for the ROK Group between 2007 and 2009 and was involved in the development and implementation of the project. Prior to commencement of this review and re-analysis, approval was given by the UNSW Human Research Ethics Committee. Prior to commencing the review of these data, London South Bank University (LSBU) Research Ethics Committee was given copies of the ROK Group application to UNSW Humans Research Ethics Committee, the issues raised by the committee, the ROK Group response and the final approval. These documents were reviewed by the LSBU Research Committee and permission was given to proceed with the review and re-analysis.

The original study was a prospective randomised controlled crossover design trial. Thirty-two myopic children of East Asian background, eight to 16 years old, were enrolled. They wore overnight orthokeratology lenses in one eye only for six months. The other eye was corrected during the day with a standard design rigid gas permeable contact lens. After six months of lens wear the lens/eye combination was reversed and lens wear continued for a further six months. Due to the unusual nature of the original study design, accommodation and binocular vision function was closely monitored throughout the study to ensure that good function remained.

Myopic progression was monitored by non-contact ocular axial length measurement with the IOLMaster (Zeiss, Germany) and automated refraction using the Shin-Nippon NVision-K 5001 autorefractor (Tokyo, Japan). Axial length was used as a proxy for myopic progression as orthokeratology lens wear alters the corneal shape in such a way that the underlying refraction cannot be determined. The residual refraction is also variable during the day (Swarbrick, 2006). An approximation for the change in refractive error with axial length change and no compensation of other ocular components is 1.0mm change in axial length is equivalent to 3.00D refractive error change (Carroll, 1981, Grosvenor and Scott, 1991, Chau *et al.,* 2004, Atchison *et al.,* 2004).

Due to the unusual nature of the modality of lens wear (an orthokeratology lens in one eye and a standard rigid gas permeable lens in the other) the selection criteria for enrolment in the study included an accommodation and binocular vision function screening. This was felt important as the lens wear could compromise accommodation and binocular vision function if it was not within normal limits at the commencement of the study. These accommodation and binocular vision function data have not previously been analysed and detailed analysis is presented here.

At the baseline measurement visit prior to lens wear and throughout the study standard accommodation and binocular vision tests were carried out. Accommodation and binocular vision tests that were performed included:

- Lag of accommodation at 40cm using the cross-cylinder technique (see Appendix C.4.1)
- Corrected distance and near phoria (at 40cm) using prism dissociation (Von Graefe method) (see Appendix C.1.20)
- Gradient AC/A ratio at near (40cm) using +1.00D, +2.00D, −1.00D and −2.00D spherical lenses (see Appendix C1.1)
- Accommodative facility with ±2.00D flipper lenses at a working distance of 40cm for one minute (see Appendix C0)
- Negative and positive relative accommodation at near using N8 test type at 40cm. First blur was taken as the endpoint (see Appendix C0)
- Stereopsis using the Randot Stereo Test Mark 1 (see Appendix C1.1)

Previous studies of optical correction and myopia control have found an association between initial binocular vision status and efficacy of treatment. Subjects with near esophoria at baseline (Fulk *et al.,* 2000, Hasebe *et al.,* 2008), increased lag of accommodation (Hasebe *et al.,* 2008) and a combination of esophoria at near and increased lag of accommodation (Gwiazda *et al.,* 2004) had a greater treatment effect.

This re-analysis of the previous study was developed to help identify any possible variables of interest for future studies in my research as it did not set out to investigate the effect of the initial binocular vision status on myopia progression.

4.2 Method

Participants who showed the most growth in axial length in the orthokeratology lens wearing eye in the first six months of lens wear only were identified and grouped. A cut off equivalent to the reported mean annual axial length growth of 0.10mm per year in emmetropic eyes was used (Mutti *et al.,* 2007), that is 0.05mm growth in the 6-month period of the study. These were labelled the ‘orthokeratology non-responders’ group. A second group was created by identifying those who had the least growth in axial length (or reduction in axial length; possibly indicating reversal of myopia), the ‘orthokeratology strong responders’ group. The cut off for this group was −0.08mm as there appeared to be a break in the data. The baseline binocular vision status of each of these groups was compared using t-tests.

For comparative purposes, those participants whose response fell between these two groups were also identified.

A similar comparison was conducted with the rigid gas permeable lens wearing control eye. However, over 14 patients exhibited axial length growth greater than the equivalent of 0.10mm per year. To separate the groups sufficiently and make comparisons a higher cut off of an equivalent growth in one year of 0.16mm was used (that is 0.08mm growth in the 6-month period of the study). Groups were labelled as the ‘RGP progressing’ group and the ‘RGP non-progressing’ group.

Given the exploratory nature of this study, differences between the groups were considered of interest if $p \leq 0.10$. Data were assessed for normality using the Shapiro-Wilk test. Depending on normality of data, post-hoc unpaired t-tests or Wilcoxon tests (WSR) were used to analyse differences.

Individual baseline binocular vision variables of interest that were identified in Study 1 were graphed against change in axial length at six months. Lines of best fit were graphed using Microsoft Excel, and correlation (R) and coefficient of determination (R^2) were also obtained using this programme.

Accommodation and binocular vision test results obtained throughout the study with lens wear were not used in this analysis due to the unusual nature of the correction.

4.3 Results

4.3.1 Orthokeratology lens wear

Six participants were included in the ‘orthokeratology non-responders’ group. These were participants that had the most increase in axial length over the first six months of orthokeratology lens wear and represent those participants who did not respond to myopia progression control treatment with the orthokeratology lens. The age range of this group was from 10.5 to 15.4 years, mean 12.7 ± 1.9 years. The mean axial length of this group at baseline was 24.30mm. The average axial length change at six months was 0.10 ± 0.05mm (range 0.05 to 0.18mm).

Eight participants were included in the ‘orthokeratology strong responders’ group. These were the participants who responded maximally to orthokeratology in terms of inhibition of axial length growth over the first six months of lens wear and represent those participants who responded to myopia progression control treatment with orthokeratology lenses. All participants in this group showed a decrease in axial length at six months compared to baseline. The age range of this group was from 10.8 to 16.6 years, mean 13.3 ± 2.3 years. This age distribution was not statistically significantly different to the ‘orthokeratology non-responders’ group (t-test, $p = 0.3$). The mean axial length of this group at baseline was 25.01mm. The mean axial length change at six months was −0.12 ± 0.01mm (range −0.17 to −0.08mm) (Table 4-1).

Excluded from either of these groups were 12 participants (‘orthokeratology mid-range responders’) who showed minimal or no axial length change over the first six months of lens wear. The age range of this group was from 10.9 to 16.0 years, mean 13.3 ± 1.7 years. Baseline axial length was 24.75mm. The mean change in axial length of the excluded participants was −0.02 ± 0.03mm (range −0.07 to 0.03mm). These participants were not included in the analysis and comparison was made between the 'orthokeratology strong responders' group and the 'orthokeratology non-responders' groups only.

There was a statistically significant difference in axial length change at six months between the two groups (t-test, $p < 0.01$). No other variable showed a statistically significant difference at the $p < 0.05$ level between the two groups. However, p values were ≤ 0.10 for the baseline binocular vision variables of lower accommodative facility (t-test, $p = 0.09$), higher AC/A (t-test, $p = 0.10$) and lower lag of accommodation (t-test, $p = 0.10$) in the 'orthokeratology non-responders' group.

Also of interest is the observation that the initial axial length was slightly shorter in the 'orthokeratology non-responders' group, although this failed to reach statistical significance ($p = 0.08$).

4.3.2 Rigid gas permeable lens wear

Nine participants were included in the 'RGP non-progressing' group. These were participants that showed the least change in axial length over the first six months of rigid gas permeable lens wear. The age range for this group was 10.5 to 16.0 years, mean 13.0 ± 2.0 years. There was no statistically significant difference in age between the two groups (t-test, $p = 0.4$). The mean axial length of this group at baseline was 24.53mm. The average axial length change at six months was −0.05 ± 0.02mm (range −0.08 to −0.03mm) (Table 4-2).

Eight participants were included in the 'RGP progressing' group. These were participants who showed the most increase in axial length over the first six months of rigid gas permeable lens wear. The age range for the 'RGP progressing' group was 11.6 to 16.6 years, mean 13.2 ± 1.7 years. The mean axial length of this group at baseline was 24.91mm. The average axial length change at six months was 0.15 ± 0.05mm (range 0.10 to 0.21mm).

Excluded from either of these groups were 10 participants as they showed smaller or no change in axial length over the initial six months of lens wear. The age range of this group was 10.9 to 16.7 years, mean 13.2 ± 2.3 years. The mean change in axial length of the excluded participants was 0.04 ± 0.03mm (range −0.02 to 0.07mm). These participants were not included in the analysis and comparison was made between the 'RGP non-progressing' group and the 'RGP progressing' groups only.

There was a statistically significant difference in axial length change at six months between the two groups (t-test, $p < 0.01$). Four other variables showed a statistically significant difference between the two groups. The baseline measurements of the 'RGP progressing group' exhibited greater exophoria at near (t-test, $p = 0.02$), lower AC/A ratio (t-test, $p = 0.04$), lower negative relative accommodation (t-test, $p = 0.04$) and higher positive relative accommodation (t-test, $p = 0.08$).

In the orthokeratology lens wearing participants that showed the greatest myopic progression ('Orthokeratology non-responders') areas of possible association included higher AC/A ratio, lower lag of accommodation and lower accommodative facility. In contrast, for the rigid gas permeable lens wearing eye the accommodation and binocular vision functions that were associated with greatest progression ('RGP progressors') were more exophoria at near, lower AC/A ratio, lower negative relative accommodation and higher positive relative accommodation.

Table 4-1

	Orthokeratology strong responders n=8 mean ± SD (range)	Orthokeratology mid-range responders n=12 mean ± SD (range)	Orthokeratology non-responders n=6 mean ± SD (range)	p-value
Change in axial length (mm)	−0.12 ± 0.01 (−0.17 to 0.08)	−0.02 ± 0.03 (−0.07 to 0.03)	0.10 ± 0.05 (0.05 to 0.18)	<0.01
Initial axial length (mm)	25.01 ± 0.84 (23.55 to 26.26)	24.75± 0.80 (23.52 to 26.51)	24.30 ± 0.73 (22.97 to 25.10)	0.08
Near phoria($^{\Delta}$)	1 ± 8 (−8 to 12)	−3 ± 5 (−9 to 4)	−1 ± 3 (−7 to 2)	0.35
Gradient AC/A	3.4 ± 1.1 (1.5 to 6)	3.6 ± 1.7 (1.5 to 6)	4.8 ± 1.7 (3 to 7)	0.10
Lag of accommodation (D)	0.50 ± 0.29 (0 to 1.00)	−0.02 ± 0.48 (−1.00 to 0.50)	0.21 ± 0.46 (−0.50 to 0.75)	0.10
Negative relative accommodation (D)	2.31 ± 0.50 (1.25 to 2.50)	2.15 ± 0.39 (1.5 to 2.50)	2.54 ± 0.10 (2.50 to 2.75)	0.36
Positive relative accommodation (D)	−1.91 ± 0.37 (−1.00 to −3.00)	−2.29± 0.65 (−1.00 to −3.00)	−1.83 ± 1.14 (0 to −3.00)	0.44
Accommodative facility (CPM)	8 ± 2 (3 to 10)	10 ± 4 (5 to 20)	6 ± 2 (4 to 9)	0.09
Stereopsis (Seconds Arc)	37 ± 7 (20 to 50)	40 ± 7 (25 to 50)	37 ± 5 (30 to 40)	0.46

Baseline binocular vision characteristics in orthokeratology lens wearing participants grouped into those showing the greatest myopic progression (non-responders) and those showing the least myopic progression (responders) after six months of lens wear. A third group of orthokeratology mid-range responders are those that were between the other two groups. They were not included in the statistical analysis. For near phoria, negative values indicate exo and positive eso.

Table 4-2

	Non-progressing RGP n=9 mean ± SD (range)	RGP mid-range responders n=9 mean ± SD (range)	RGP progressors (non-responders) n=8 mean ± SD (range)	p-value
Change in axial length (mm)	−0.05 ± 0.02 (−0.08 to −0.03)	0.04 ± 0.03 (−0.02 to 0.07)	0.15 ± 0.05 (0.10 to 0.21)	<0.01
Initial axial length (mm)	24.53 ± 0.92 (23.05 to 26.26)	22.52 ± 7.45 (23.28 to 25.62)	24.91 ± 1.06 (23.35 to 26.26)	0.23
Near phoria (Δ)	0 ± 5 (−8 to 9)	1 ± 5 (−7 to 12)	−6 ± 4 (−9 to 2)	0.02
Gradient AC/A	4.3 ± 1.8 (1.5 to 7.0)		2.7 ± 0.8 (2.0 to 4.0)	0.05
Lag of accommodation (D)	0.25 ± 0.43 (−0.50 to 0.75)	0.18 ± 0.55 (−0.25 to 1.00)	0.08 ± 0.47 (−0.75 to −0.50)	0.32
Negative relative accommodation (D)	2.44 ± 0.21 (2.00 to 2.75)	2.25 ± 0.47 (1.25 to 2.50)	2.14 ± 0.40 (1.50 to 2.50)	0.05
Positive relative accommodation (D)	−1.64 ± 0.87 (0 to −3.00)	−2.30 ± 0.63 (−1.25 to −3.00)	−2.29 ± 0.81 (−1.00 to −3.00)	0.08
Accommodative facility (CPM)	8 ± 3 (3 to 15)	8 ± 5 (4 to 20)	9 ± 3 (6 to 14)	0.29
Stereopsis (Seconds arc)	39 ± 6 (30 to 50)	39 ± 7 (25 to 50)	37 ± 10 (20 to 50)	0.50

Baseline binocular vision characteristics in rigid gas permeable lens wearing participants grouped into those showing the greatest myopic progression (progressing) and those showing the least myopic progression (non-progressing) after 6 months of lens wear. A third group of rigid gas permeable mid-range responders are those that were between the other two groups. They were not included in the statistical analysis. For phoria, negative values indicate exo and positive eso.

4.3.2.1 AC/A ratio

Baseline data for AC/A ratio were available in 16 participants. A scatter plot of AC/A ratio and change in axial length in the orthokeratology lens wearing eye can be found in Figure 4-1. A scatter plot of AC/A ratio and change in axial length in the rigid gas permeable lens wearing eye can be found in Figure 4-2.

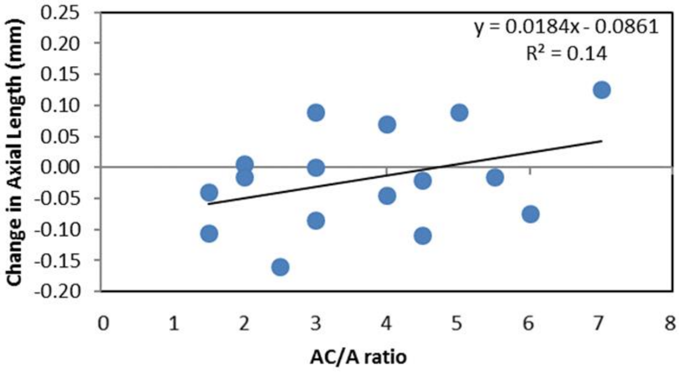

Figure 4-1 Baseline AC/A ratio versus the change in axial length in the orthokeratology lens wearing eye at six months. Solid line is the linear regression line.

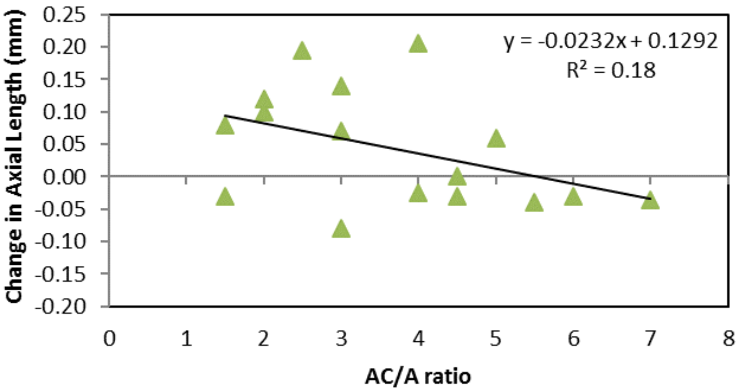

Figure 4-2 Baseline AC/A ratio versus the change in axial length in the rigid gas permeable lens wearing eye at 6 months. Solid line is the linear regression line.

There appeared to be a slight trend for higher baseline AC/A ratios to be associated with greater axial length growth in the orthokeratology lens wearing eye while there was an opposite effect in the rigid gas permeable lens wearing eye. These results suggest that orthokeratology lens wear may have a more profound effect on those with low AC/A ratios, who may otherwise have progressed more in myopic refractive error.

4.3.2.2 Lag of accommodation

Baseline data were available for 25 participants. A scatter plot of AC/A ratio and change in axial length in the orthokeratology lens wearing eye can be found in Figure 4-3. A scatter plot of AC/A ratio and change in axial length in the rigid gas permeable lens wearing eye can be found in Figure 4-4.

There appears to be a slight trend towards greater axial length growth with lower lag of accommodation in the orthokeratology lens wearing eye while initial lag of accommodation did not appear to influence the rate of axial length change in rigid gas permeable lens wearing eyes.

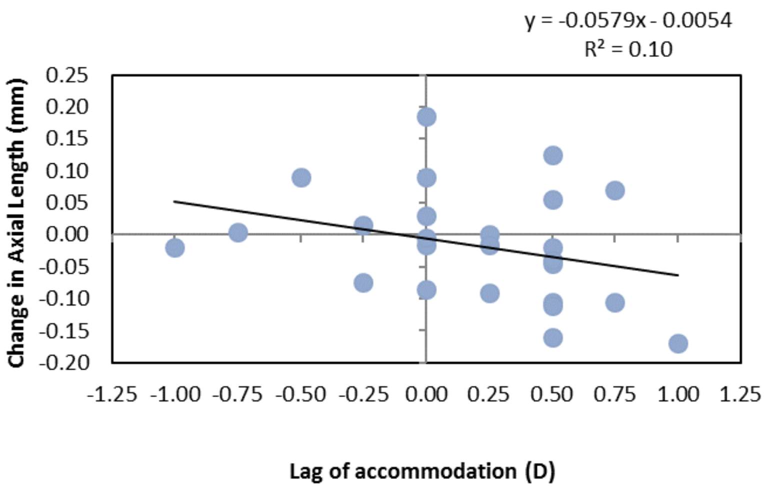

Figure 4-3 Baseline accommodative lag versus the change in axial length in the orthokeratology lens wearing eye at six months. Solid line is the linear regression line.

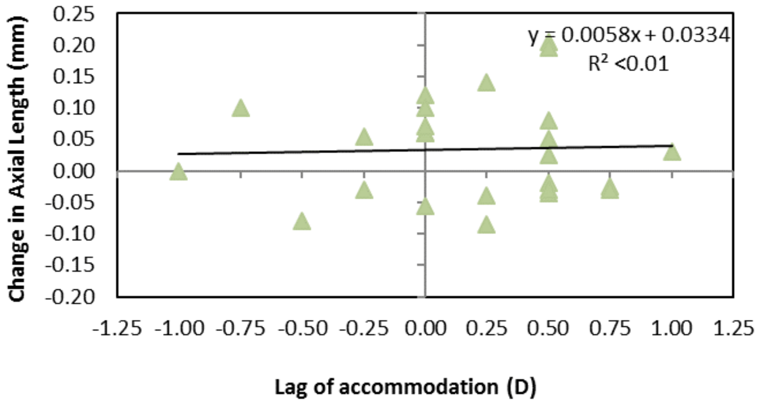

Figure 4-4 Baseline accommodative lag versus the change in axial length in the rigid gas permeable lens wearing eye at six months. Solid line is the linear regression line.

4.3.2.3 Accommodative facility

All participants (n = 26) had data for initial accommodative facility. No associations were apparent between the initial accommodative facility and change in axial length in either orthokeratology or rigid gas permeable lens wearing eyes.

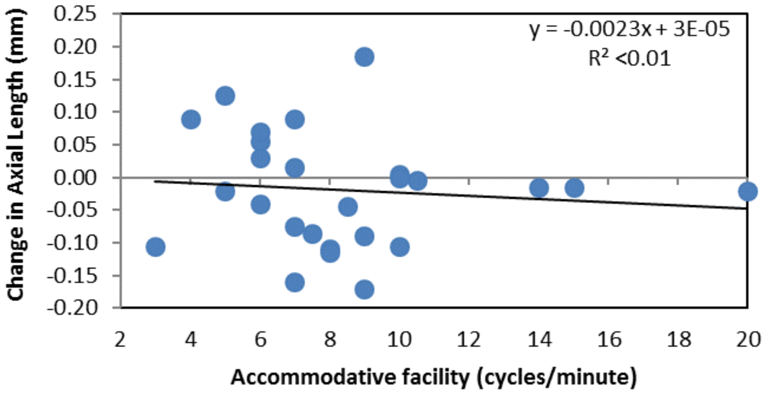

Figure 4-5 Baseline accommodative facility versus the change in axial length for the orthokeratology lens wearing eye at six months. Solid line is the linear regression line.

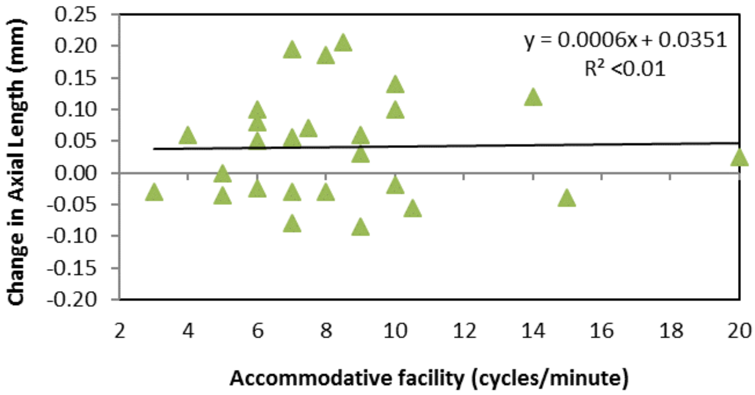

Figure 4-6 Baseline accommodative facility versus the change in axial length in the rigid gas permeable lens wearing eye at six months. Solid line is the linear regression line.

4.3.2.4 Negative and positive relative accommodation

All participants had baseline data available. There appears to be no association with baseline positive relative accommodation and axial length in orthokeratology lens wear. In keeping with the earlier findings of this study, lower positive relative accommodation may be associated with less axial length growth, although this association is likely to be small. For scatter plots of positive relative accommodation see Figure 4-7 and Figure 4-8.

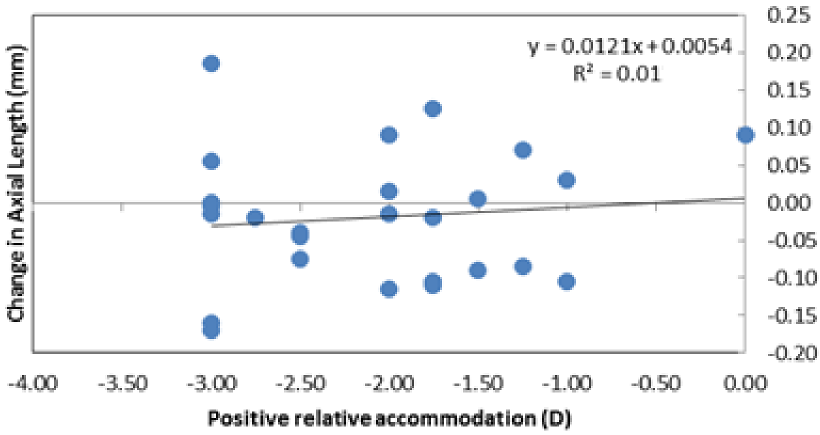

Figure 4-7 Baseline positive relative accommodation versus the change in axial length for the orthokeratology lens wearing eye at six months. Solid line is the linear regression line.

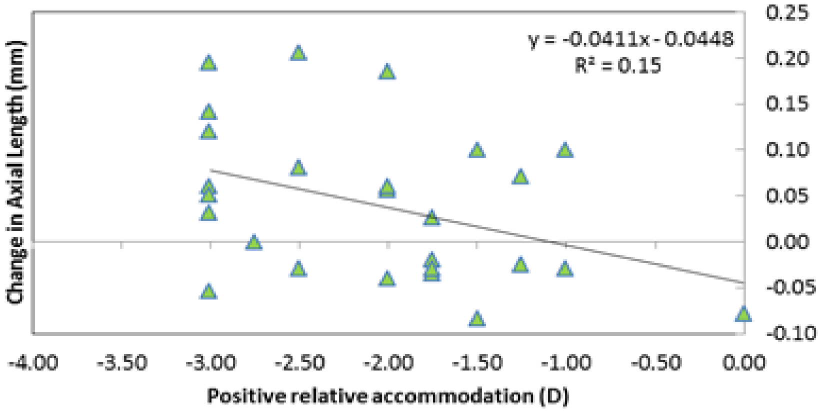

Figure 4-8 Baseline positive relative accommodation versus the change in axial length for the rigid gas permeable lens wearing eye at six months. Solid line is the linear regression line.

There appears to be very little association between change in axial length and baseline negative relative accommodation for either orthokeratology or rigid gas permeable lens wearing eyes. For scatter plots of positive relative accommodation see Figure 4-9 and Figure 4-10.

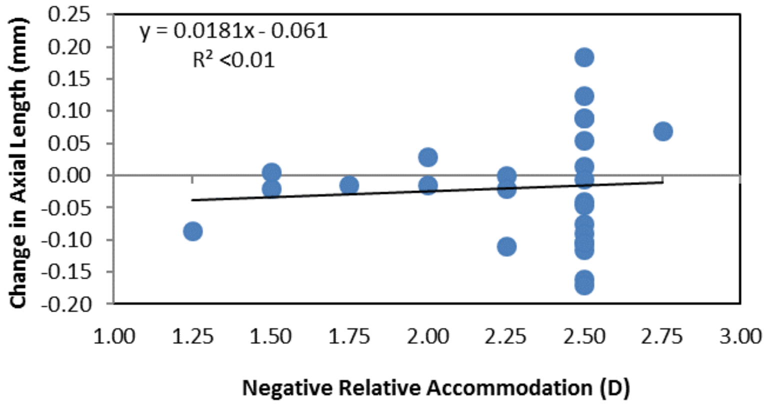

Figure 4-9 Baseline negative relative accommodation versus the change in axial length for the orthokeratology lens wearing eye at six months. Solid line is the linear regression line.

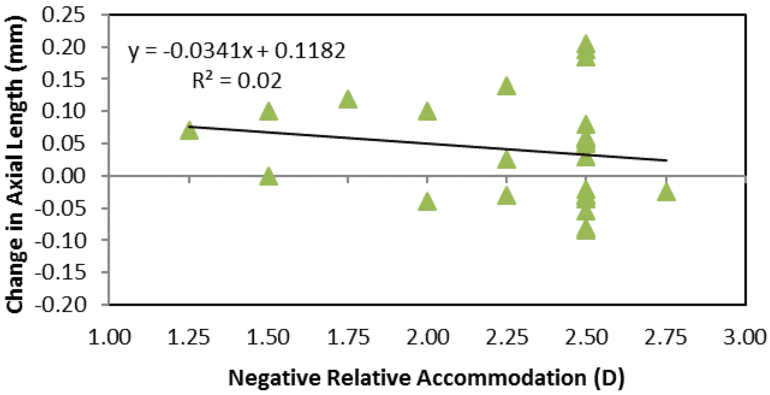

Figure 4-10 Baseline negative relative accommodation versus the change in axial length for the rigid gas permeable lens wearing eye at six months. Solid line is the linear regression line.

Both positive and negative relative accommodation had clusters of points at 2.50D. For negative relative accommodation patients focussing at a working distance of 40cm have an accommodative demand of −2.50D. Any lenses of higher power than this should induce blurred vision if the distance refraction is fully corrected. For negative relative accommodation, the expected norm is +2.50D. The examiner may have not tested further than this level, as they were determining if the participant had normal accommodation and binocular vision function, and testing beyond this point would not give any useful additional information.

4.3.2.5 Near phoria

There was no association between baseline near phoria and axial length growth in the orthokeratology lens wearing eye.

There was a slight association between baseline near phoria and axial length growth in the rigid gas permeable lens wearing eye, with participants with exophoria showing greater axial length growth.

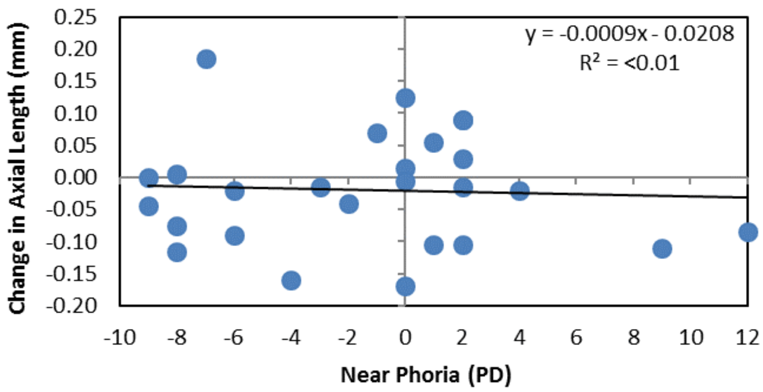

Figure 4-11 Baseline near phoria versus the change in axial length for the orthokeratology lens wearing eye at six months. Negative values indicate exo and positive eso. Solid line is the linear regression line.

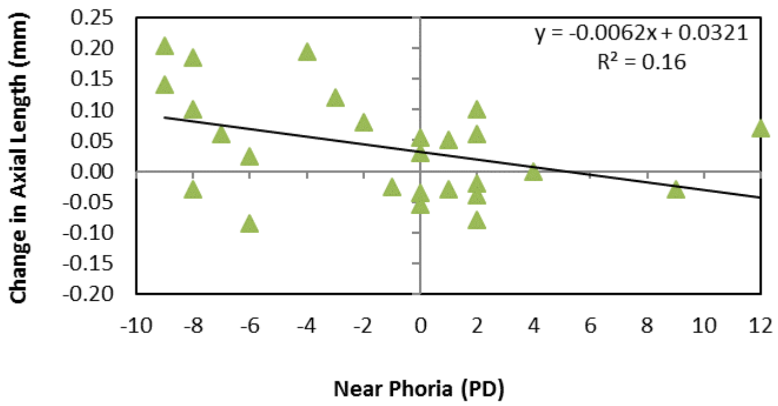

Figure 4-12 Baseline near phoria versus the change in axial length for the rigid gas permeable lens wearing eye at six months. Negative values indicate exo and positive eso. Solid line is the linear regression line.

4.3.3 Additional analysis

The baseline binocular vision parameters of near phoria and lag of accommodation were further investigated as there are several reports in the myopia control literature that these may influence myopic progression.

4.3.3.1 Near phoria

Goss and Jackson (1996) noted that the presence of near phoria which is not close to orthophoria (zero) is a risk factor for the development of myopia. In this study, the cohort was divided into 'low near phoria' (n = 8), and 'high near phoria' (n = 18) for both the orthokeratology lens wearing eye and the rigid gas permeable eye. Low near phoria was defined as 1^{Δ} esophoria to 2^{Δ} exophoria while high near phoria was outside this range. The average axial length change at three and six months was plotted for each group.

There was no statistically significant difference in axial length change between the low near phoria group and the high near phoria group in the orthokeratology lens wearing eye (t-test, p = 0.33) or the rigid gas permeable lens wearing eye (t-test, p = 0.11). This is in contrast to Goss and Jackson (1996) who showed that near phoria that is not close to ortho is predictive of myopia progression. Figure 4-13 does reveal some interesting trends that are worthy of further investigation with larger sample sizes and more orthodox orthokeratology lens wear.

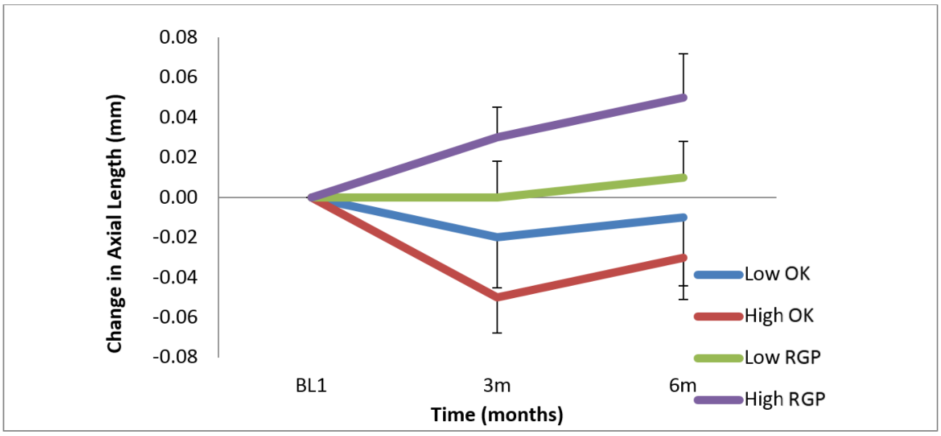

Figure 4-13 Change in axial length from baseline at three and six months. Participants were grouped by baseline near phoria and lens wear. Error bars are the standard error of the mean.

4.3.3.2 Lag of accommodation

The cohort was then divided into 'high lag' (greater than +0.50D) (n = 11) and 'low lag' (+0.50D or less) (n = 15) for both the orthokeratology lens wearing eye and the rigid gas permeable eye. The mean axial length change at three and six months was plotted for each group.

There was no statistically significant difference in axial length change between the high lag group and the low lag group in the orthokeratology lens wearing eye (t-test, p = 0.10) or the rigid gas permeable lens wearing eye (t-test, p = 0.49).

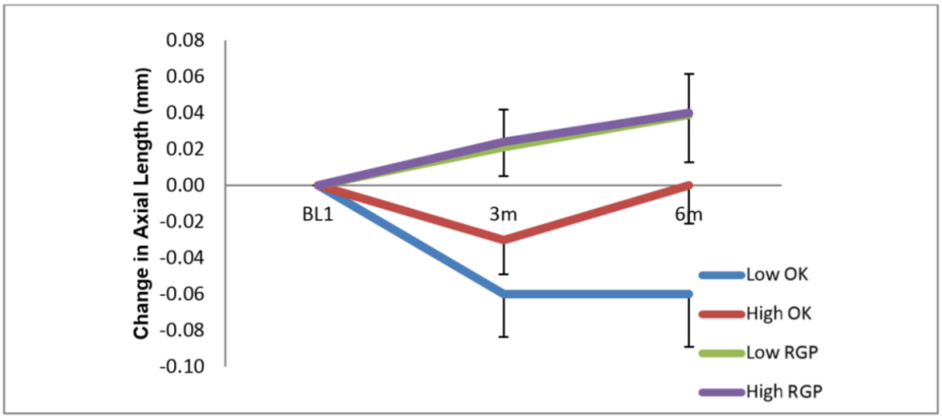

Figure 4-14 Change in axial length from baseline at three and six months. Participants were grouped by baseline lag of accommodation and lens wear. Error bars are the standard error of the mean.

4.3.3.3 Stereopsis

It was possible that the apparent difference between the 'low phoria' and 'not low phoria' group in the rigid gas permeable lens wearing eye may be the result of a breakdown of stereopsis with the unusual lens wearing modality. However, there appeared to be no association between the change in stereopsis and change in axial length. This was for either the orthokeratology or the rigid gas permeable lens wearing eye. In addition there was no association between the change in stereopsis and change in axial length at any of the measurement visits. The six-month visit results are shown below (Figure 4-15).

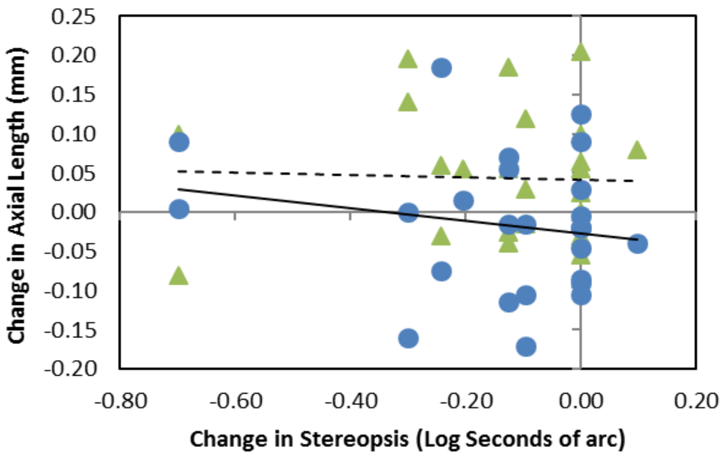

Figure 4-15 Change in stereopsis from baseline versus change in axial length for rigid gas permeable lens and orthokeratology lens wear. Green triangles indicate rigid gas permeable lens wear. Blue circles indicate orthokeratology lens wear. Solid line is the linear regression line for orthokeratology lens wear. Dashed line is the linear regression line for rigid gas permeable lens wear.

4.4 Discussion

This study (Study 1) was conducted to identify possible variables of interest to further investigate in later studies of my research.

In the orthokeratology lens-wearing eye these variables included accommodative facility which was higher (closer to normal) in those that responded best to orthokeratology lens myopia progression control treatment than those that did not respond (t-test, $p = 0.09$), AC/A ratio which was lower (closer to normal) in the responders than those that did not respond (t-test, $p = 0.10$), and lag of accommodation which was higher (closer to normal) in the responders compared to those that did not respond (t-test, $p = 0.10$). Although these variables failed to reach statistical significance at the $p < 0.05$ level they still warrant further investigation.

Although there were individual variations, as a group the orthokeratology responders appeared on average to have binocular vision status closer to normal than the non-responding group.

Interestingly, baseline near phoria did not appear to be associated with response to treatment with orthokeratology lens wear. This is different from bifocal spectacle lens wear studies that show that initial near phoria is associated with the efficacy of treatment.

This difference in response could indicate that the orthokeratology control effect may be more because of changes to relative peripheral refraction with orthokeratology lens wear, rather than changes in the accommodative or binocular vision status.

The results of this study suggest that when a participant's initial accommodative facility is poor the treatment effect with orthokeratology lenses is reduced. In orthokeratology lens wear, there is some variation in refraction throughout the day. Participants with reduced accommodative facility may have found adjusting to the different accommodative requirements difficult and may not have been able to sustain clear accurate vision. Alternatively, O'Leary and Allen (2001) have shown that accommodative facility is lower in myopes than emmetropes when measured at distance. Allen and O'Leary (2006), in a prospective study of university aged students, found that accommodative facility was an independent predictor of myopia progression. The participants in this study who had reduced baseline accommodative facility may represent those at risk of faster myopic progression, reducing the treatment effect of orthokeratology.

Baseline AC/A ratios were higher in the non-responders group in orthokeratology lens wear. Jiang (1995) noted higher AC/A ratios in emmetropes who became late onset (college student) myopes than in those who remained emmetropic. A prospective study by Mutti and colleagues (2000) also showed that those participants with higher baseline

AC/A ratios were at increased risk of myopic progression. If those participants with higher baseline AC/A ratios were at risk of more rapid myopic progression, the treatment effect with orthokeratology may be less obvious.

In the rigid gas permeable lens-wearing eye there was an apparent opposite trend with lower baseline AC/A ratios associated with greater axial length increase.

There have been variable reports of the effect of lag of accommodation on myopia progression. Allen and O'Leary (2006) found that lag of accommodation was an independent predictor of myopia progression, whereas Weizhong and colleagues (2008) found no association. In this study, although the lag of accommodation was on average normal in the responders to orthokeratology lens wear there was a lower lag with a tendency towards a lead of accommodation in the non-responders.

Also, there was a small, but not statistically significant (t-test, $p = 0.08$) difference in the initial axial length between the 'progressing' versus the 'non-progressing' orthokeratology lens wearers. It may be that the 'progressing' group were growing more rapidly than the other group and the myopia progression control treatment effect was less apparent.

In rigid gas permeable lens wear the variables of interest appeared to be baseline near phoria with more exophoria in the myopia progressing group (t-test, $p = 0.02$), AC/A ratio which was lower in the rigid gas permeable lens wearers who progressed (t-test, $p = 0.04$), negative relative accommodation which was also lower in the rigid gas permeable lens wearers who progressed (t-test, $p = 0.04$) and positive relative accommodation which was higher in the rigid gas permeable progressing group (t-test, $p = 0.08$). These findings contrast with those of the orthokeratology lens wear eye suggesting that baseline accommodation and binocular vision function may play a role in myopia progression in the absence of myopia progression control treatment.

4.4.1 Future directions

This study (Study 1) has identified that binocular vision status may have some influence on the myopia progression control treatment effect of orthokeratology lenses. Further investigation along these lines appears warranted. It should be noted that the participants in this phase were initially screened for binocular vision status for inclusion in the study and thus represent a group of participants with binocular vision status closer to normal than is likely to be the case in a random cross-section of myopes.

The next study described in this thesis is a retrospective review of data from private practice. Based on the results of Study 1 primary variables of interest will include accommodative facility, AC/A ratio and lag of accommodation. As the next study also aims to determine if there is any change in binocular vision function after wearing orthokeratology lenses, change in stereopsis will also be investigated.

Study 1 identified the difficulty of analysing variables that have an expected value. For example, the expected value of negative relative accommodation at 40cm is +2.50D. In this instance it may be more useful to analyse these data as nominal (that is, categorising the data as normal or abnormal).

4.4.2 Limitations

This study was carried out with an unusual lens wearing modality. Orthokeratology lenses were worn overnight in one eye while the other eye wore a rigid gas permeable lens during the day. The influence of this lens-wearing modality on everyday binocular vision status is unclear, but it may have had an adverse effect due to the different optical properties between the two lens types.

The sample size chosen for this study was calculated based on expected changes in axial length. A larger sample size may be required to take into account the greater variability in initial binocular vision status and the repeatability of testing in future studies.

The groups (responders versus non-responders) were not matched for age or initial refractive error which may influence myopic progression.

This study screened for (relatively) normal binocular vision status prior to entry as a subject. Further studies could usefully include participants with the wide range of accommodation and binocular vision status that is found in the general population.

5 The impact of orthokeratology lens wear on accommodation and binocular vision in community optometric practice

5.1 A retrospective analysis of clinical data from two practices

This chapter (Study 2) aims to investigate whether orthokeratology lens wear alters accommodation and binocular vision function. It is a retrospective analysis of clinical data taken from the patient records of two private optometric practices in Australia and compares accommodation and binocular vision function at baseline and during orthokeratology lens wear.

5.2 Introduction

This study (Study 2) aimed to identify if accommodation and binocular vision status alters with orthokeratology lens wear. It used quantitative research methods throughout. It is a retrospective review of the accommodation and binocular vision data from orthokeratology lens wearers in two private optometric practices in Australia. These data were obtained under typical clinical conditions and not under controlled experimental conditions that applied to the data described in the last chapter. The data described in this chapter were more naturalistic in that, in contrast to Study 1, both eyes received the same treatment in every case.

5.3 Background

In Chapter 4 of this thesis, the following observations were made:

Orthokeratology lenses appeared to have the greatest treatment effect when the initial binocular vision status is close to population norms, in particular:

- Accommodative facility
- AC/A ratios
- Lag of accommodation.

In contrast, with poor accommodative facility there was a decreased treatment effect and AC/A ratios were higher and lag of accommodation was lower in those who did not respond to orthokeratology treatment.

There was a small difference in average initial axial length between progressing versus non-progressing orthokeratology lens wearers. Axial length growth was greatest over the study period in those with smaller initial axial length (t-test, $p = 0.08$).

Conventional rigid gas permeable lenses (the control condition) led to the greatest axial length growth when:

- The initial near phoria was more exo
- Negative relative accommodation was lower and positive relative accommodation was higher
- There was a lower initial AC/A ratio.

Previous research on the correlation between orthokeratology lens wear and oculomotor balance has been equivocal. Some studies have found orthokeratology lens wear is associated with improved near accommodative facility (Brand, 2013), decreased lag of accommodation (Tarrant, 2009, Brand, 2013), decreased AC/A (Brand, 2013) and an increase in negative relative accommodation after three months and three years of lens wear (Felipe-Marquez *et al.,* 2015). Orthokeratology has also been reported to induce a small but not statistically significant shift in the exo direction in near phoria after three months of lens wear (Brand, 2013, Felipe-Marquez *et al.,* 2016).

However, other studies have demonstrated no significant changes with orthokeratology lens wear in distance phoria (Felipe-Marquez *et al.,* 2016), near phoria (McLeod, 2006), lag of accommodation (McLeod, 2006, Felipe-Marquez *et al.,* 2015), positive and negative relative accommodation (McLeod, 2006), accommodative facility (McLeod, 2006) or monocular accommodative facility (Felipe-Marquez *et al.,* 2015).

5.4 Method

This study (Study 2) is a retrospective analysis of the clinical findings of orthokeratology lens wearers by two optometrists in private practice in Australia. Prior to commencement of the study, approval was given by UNSW Human Research Ethics Advisory Panel and subsequently The Institute of Optometry and LSBU gave approval of the study by Research Ethics Committee Chairs' Action.

Two Australian optometrists, (SD, Penshurst, NSW and MM, Canberra, ACT) supported the research. They identified all patients fitted with orthokeratology lenses from 2010 to 2012 in their practices. Patient data were de-identified (anonymised) by the optometrist and sent to me. De-identified patient records were assigned a study number and data of interest were collated in an Excel spreadsheet. Data included the following:

- Refractive error before and during lens wear
- Distance visual acuity at 6m
- Age (or year at school or university) at initial fitting of lenses
- Date of commencing orthokeratology lens wear
- Orthokeratology lens design.

Accommodation and binocular vision tests included in data collection before and during orthokeratology lens wear were:

- Lag of accommodation at 40cm using the cross-cylinder technique (see Appendix C0)

- Corrected distance phoria at 6m and near phoria at 40cm using the Von Graefe method (see Appendix C0)
- Near accommodative facility with ±2.00D flipper lenses at a working distance of 40cm for one minute (see Appendix C0)
- Stereopsis using the Titmus Stereo Test (see Appendix C1.1)
- Gradient AC/A ratio at near (40cm) using +1.00D, +2.00D −1.00D and −2.00D spherical lenses (see Appendix C1.1)
- Negative and positive relative accommodation at near using N8 test type at 40cm. First blur was taken as the endpoint (see Appendix C0)
- Distance (6m) and near (40cm) fusional reserves using Risley prisms (see Appendix C0).

Lines of best fit were graphed using Microsoft Excel, and Pearson correlation co-efficient (R) was also obtained using this programme. Data were assessed for normality using the Shapiro-Wilk test. If normally distributed, post-hoc paired t-tests were used to analyse changes in mean values. For data that was not normally distributed, the Wilcoxon (WSR) test was used. Changes in the standard deviation or variance were also tested using the F test. A p-value of <0.05 was taken to be statistically significant.

5.5 Results

5.5.1 Practice 1

Nineteen patients were included in the analysis. Mean age at commencement of lens wear was 12.2 ± 2.5 years (range 7.8 to 17.2 years).

There was a statistically significant reduction in refractive error during lens wear ($p < 0.01$) in both eyes (Table 5-1).

	Right eye mean ± SD (range)	Left eye mean ± SD (range)
Pre-lens wear	−2.09D ± 0.88D (−0.75 to −4.38D)	−2.13D ± 0.81D (−1.00 to −4.38D)
During lens wear	−0.22D ± 0.44D (+0.75 to −1.00D)	−0.26D ±0.47D (+1.00 to −1.25D)

Table 5-1 Spherical equivalent refractive (SER) error at baseline and post lens wear in dioptres (D).

During lens wear mean corrected distance visual acuity was unchanged from pre-lens wear.

Orthokeratology **Practice 1**	**n**	**Baseline** mean ± SD(range)	**During treatment** mean ± SD (range)	p-value
Distance phoria (Δ)	9	−2.4 ± 5.1 (−15 to 3)	−1.5 ± 1.6 (−4.0 to 1.5)	0.59
Near phoria (Δ)	11	−1.1 ± 5.0 (−9.0 to 11)	−2.3 ± 3.2 (−8.0 to 1.5)	0.22
Lag of accommodation (D)	6	+0.21 ± 0.38 (−0.25 to +0.50)	+0.14 ± 0.14 (−0.50 to 0.50)	0.68
Accommodative facility (CPM)	6	3.6 ± 3.5 (0 to 9)	11.0 ± 4.4 (4 to 16)	0.01
Positive relative accommodation (D)	8	2.04 ± 0.82 (1.00 to 3.00)	2.60 ± 0.60 (1.50 to 3.00)	0.23
Negative relative accommodation (D)	8	2.25 ± 0.60 (1.25 to 6.00)	2.10 ± 0.40 (1.50 to 2.50)	0.61
Distance PFR break (Δ)	13	17 ± 10 (6 to 40)	17 ± 8 (4 to 25)	0.79
Distance PFR recovery (Δ)	13	7 ± 4 (1 to 15)	10 ± 4 (2 to 15)	0.08
Distance NFR break (Δ)	13	11 ± 5 (6 to 20)	8 ± 2 (4 to 12)	<0.01
Distance NFR recovery (Δ)	13	6 ± 3 (3 to 15)	5 ± 3 (2 to 10)	0.11
Near PFR break (Δ)	4	21 ± 9 (8 to 30)	18 ± 3 (15 to 20)	0.51
Near PFR recovery (Δ)	4	12 ± 2 (10 to 15)	13 ± 2 (10 to 15)	0.25
Near NFR break (Δ)	12	18 ± 4 (8 to 25)	12 ± 3 (15 to 25)	0.37
Near NFR recovery (Δ)	12	12 ± 3 (6 to 16)	15 ± 3 (10 to 20)	0.07
Gradient AC/A +1	6	2.9 ± 1.3 (2 to 4)	2.5 ± 1.4 (1 to 4)	0.56
Gradient AC/A −1	9	2.5 ± 1.4 (1 to 4)	1.8 ± 1.5 (0 to 3)	0.19

Table 5-2 Mean accommodation and binocular vision function before lens wear and during lens wear at Practice 1. For phoria, negative values indicate exo and positive eso. “PFR” indicates positive fusional reserves. “NFR” indicates negative fusional reserves.

5.5.1.1 Distance phoria

Distance phoria was measured before and during lens wear in 9 patients. A scatter plot of individual results is found in Figure 5-1. Mean distance phoria was unchanged with lens wear (t-test, p = 0.59). However, the standard deviation was reduced with lens wear (F test, p = 0.004), and range was reduced indicating patients became closer to orthophoria.

Of interest was one patient (patient 17) who showed a significant improvement in distance phoria from 15$^{\Delta}$ exophoria prior to lens wear to 2$^{\Delta}$ exophoria during lens wear.

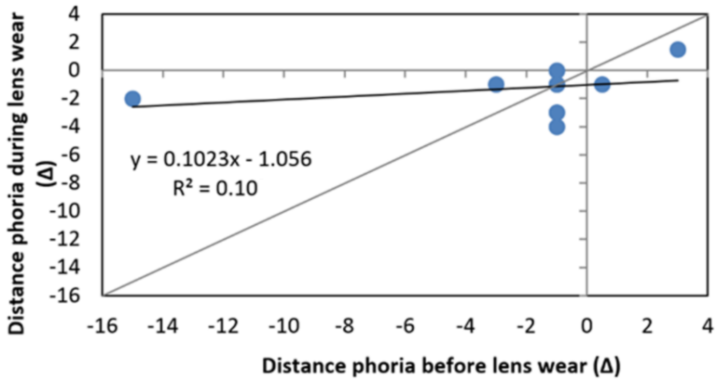

Figure 5-1 Distance phoria before lens wear compared to during lens wear in prism dioptres ($^{\Delta}$). Negative values indicate exo and positive eso. Grey line indicates 1:1 line. Solid black line is the linear regression line.

5.5.1.2 Near phoria

Near phoria was measured before and during lens wear in 11 patients. A scatter plot of individual results is shown in Figure 5-2. There was a small but not statistically significant increase in the exo direction in mean near phoria during lens wear (t-test, p = 0.22). There was a slight (but not statistically significant) reduction in standard deviation of near phoria (F test, p = 0.17) and range, suggesting more patients became closer to orthophoria with lens wear.

Of interest, one patient (patient 11) with significant phoria (11^{Δ} esophoria) prior to lens wear improved to 1.5^{Δ} esophoria with lens wear.

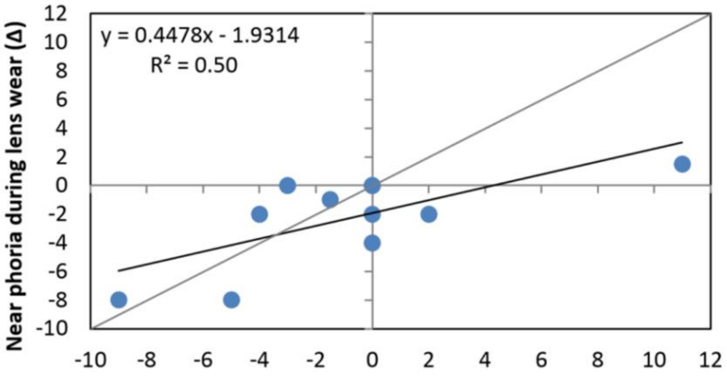

Figure 5-2 Near phoria in prism dioptres (Δ) before lens wear and during lens wear. Negative values indicate exo and positive eso. Grey line indicates 1:1 line. Solid black line is the linear regression line.

5.5.1.3 Lag of accommodation

Lag of accommodation before and during orthokeratology was measured in six patients. A scatter plot of individual results is shown in Figure 5-3.

The mean lag of accommodation was unchanged during lens wear (t-test, $p = 0.68$).

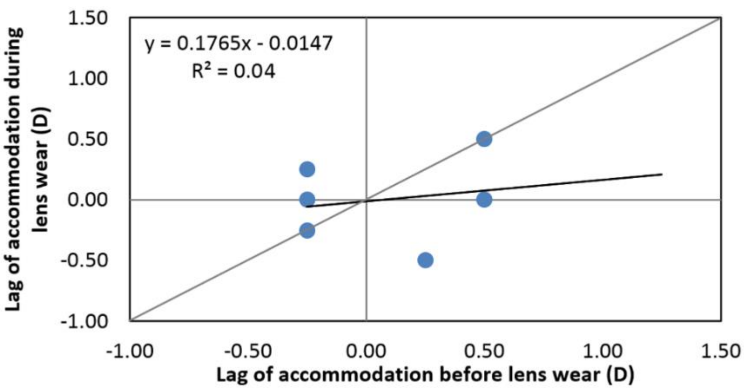

Figure 5-3 Lag of accommodation in dioptres (D) before and during lens wear. Grey line indicates 1:1 line. Solid black line is the linear regression line.

5.5.1.4 Positive and negative relative accommodation

Positive and negative relative accommodation was measured in 8 patients. Scatter plots can be seen in Figure 5-4 and Figure 5-5. There was no change in mean negative relative accommodation (t-test, p = 0.69). There was a slight increase in mean positive relative accommodation, although this failed to reach statistical significance (t-test, p = 0.23).

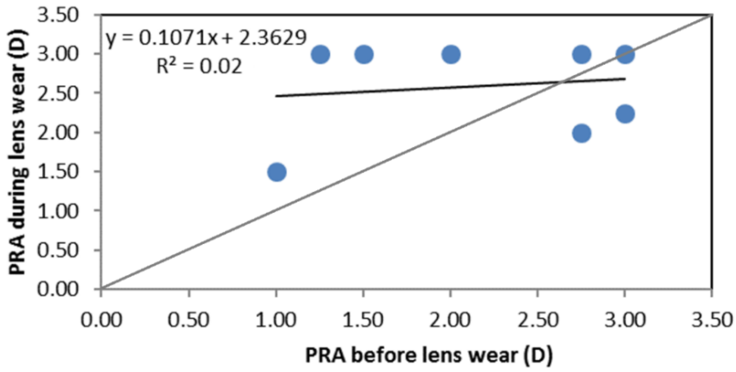

Figure 5-4 Positive relative accommodation (PRA) before and during orthokeratology lens wear. Grey line indicates 1:1 line. Solid black line is the linear regression line.

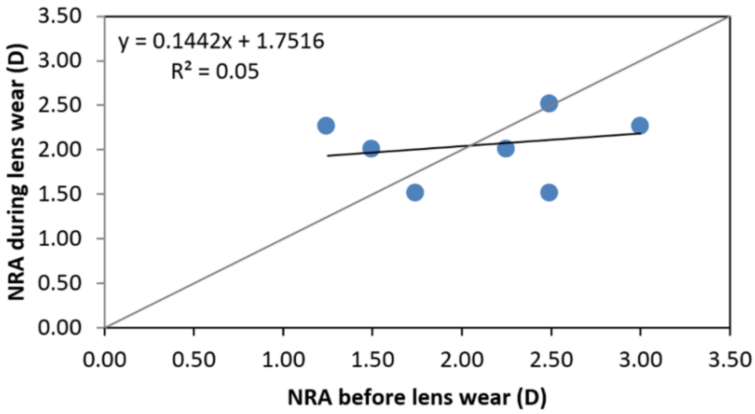

Figure 5-5 Negative relative accommodation (NRA) before and during lens wear. Grey line indicates 1:1 line. Solid black line is the linear regression line.

Mean range of clear vision increased during lens wear from 4.29 ± 1.20D (2.50 to 6.00D) to 4.71 ± 0.80D (3.00 to 5.50D), but this failed to reach statistical significance (t-test, p = 0.42).

5.5.1.5 Accommodative facility

Accommodative facility was measured before and during lens wear in six patients. Mean rate of accommodative facility increased during lens wear. This was a statistically significant difference (t-test, p = 0.01). Individual accommodative facility results are shown in Figure 5-6.

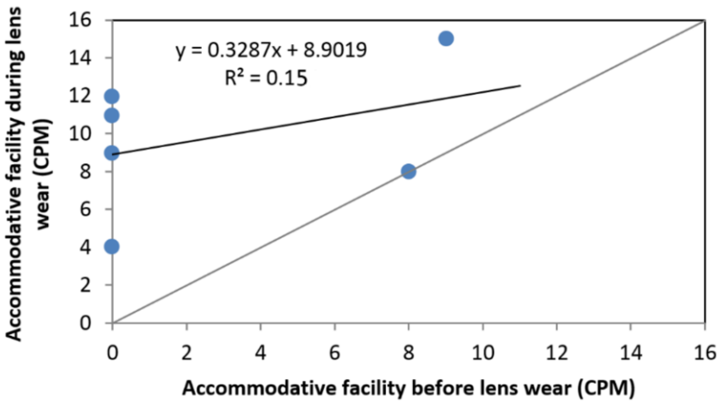

Figure 5-6 Accommodative facility results before and during lens wear in cycles per minute. Grey line indicates 1:1 line. Solid black line is the linear regression line.

There were four patients who failed accommodative facility with ±2.00D flipper lenses prior to orthokeratology lens wear. These patients showed more normal accommodative facility after orthokeratology lens wear. There were no patients who passed accommodative facility with ±2.00D flipper lenses prior to lens wear who subsequently failed following orthokeratology lens wear.

Of particular interest were two of these patients. Both failed accommodative facility testing in their first examination in Practice 1, and were then fitted with orthokeratology lenses. Patient six was first seen in Practice 1 in 2004 aged four years. Accommodative facility was not tested at this examination. In January 2006 (six years old) the patient passed ±1.50D flippers (8 cycles per minute) (note the negative and positive relative accommodation was +1.50D and −2.50D respectively). In 2007 (seven years old) accommodative facility was not retested. In January 2009 (nine years old) the patient failed clearing plus. Note the negative relative accommodation (B+) was +1.75D, and the positive relative accommodation (B-) was −3.00D. During orthokeratology lens wear in 2010 (10 years old) accommodative facility was retested using ±2.00D flipper lenses and the patient could clear 9 cycles per minute which is a reasonable result.

Patient eight was first seen in Practice 1 in March 2008 (10 years old at this visit). Accommodative facility was not tested at this visit. This patient had positive and negative relative accommodation of +1.25 and −1.00D which indicates they would not pass accommodative facility testing. In 2008 accommodative facility was not tested. In June 2009 (11 years old at this visit) accommodative facility was tested and failed. The positive and negative relative accommodation was tested but failed in the minus direction (−1.00D) indicating that they would fail accommodative facility testing. Accommodative facility testing was performed following orthokeratology lens wear in 2012 (14 years old at this visit) and was 11 cycles per minute which is within normal limits.

5.5.1.6 Fusional reserves

Distance positive fusional reserves (break and recovery) before and during lens wear were measured in 13 patients. There was not a significant change in mean break point (t-test, $p = 0.79$). There was slight improvement in mean recovery point from before lens wear, although this failed to reach statistical significance (t-test, $p = 0.08$).

Distance negative fusional reserves (break and recovery) were measured in 13 patients. There was a statistically significant reduction in mean negative fusional reserve break point ($p < 0.01$) during lens wear. Mean recovery point was also slightly reduced during lens wear, and this was close to statistical significance (t-test, p = 0.11), but the small change involved would most likely not be clinically significant.

Near positive fusional reserves (break and recovery) were measured in four patients. There was no statistically significant change in mean break point (t-test, p = 0.51) or mean recovery point during lens wear (t-test, p = 0.25).

Near negative fusional reserves (break and recovery) were measured in 12 patients. There was no statistically significant change in mean break point during lens wear (t-test, p = 0.37). There was a possible slight improvement in near recovery point mean during lens wear, however this failed to reach statistical significance (t-test, p = 0.07). Seven of these patients showed an increase in recovery point (range of improvement 2^{Δ} to 9^{Δ}), two were worse with orthokeratology lens wear (1^{Δ} and 5^{Δ}) while 3 remained unchanged.

5.5.1.7 AC/A ratio

AC/A ratios were measured in six patients before and during lens wear. Individual data used to calculate AC/A ratio are shown in Table 5-3.

Patient number	**Before lens wear AC/A** Near phoria	−2.00D	−1.00D	+1.00D	+2.00D	**During Lens wear AC/A** Near phoria	−2.00D	−1.00D	+1.00D	+2.00D
1	2	7	5	−0.5	−2	−2	0	−2	−6	−7
4	0	3	3	−4	−9	−2	0	0	−5	−7
5	−4	5	0	−6	−11	−2	2	1	−3	−5
6	0	5	3	−2	−4	0	5	3	−2	−4
16	0	4	2	−2	Too blurry	0	6	3	−1	−4
19	0	2	1	−4	−6	−4	−2	−4	−8	−8
Mean	−0.3	3.3	2.3	−3.1	−6.4	−1.7	1.8	0.2	−4.2	−5.8
SD	2.0	3.5	1.8	2.0	3.6	1.5	3.1	2.8	2.6	1.7
Max	2	7	5	−0.5	−2	0	6	3	−1	−4
Min	−4	2	0	−6	−11	−4	−2	−4	−8	−8

Table 5-3 Data used to calculate AC/A ratio. Phoria at near and with + 1.00, + 2.00, −1.00 and −2.00D lenses. Negative values indicate exo and positive eso.

Mean AC/A ratio with positive lenses was 2.7 ± 1.2 (range 1 to 4.5) prior to lens wear and was slightly reduced during lens wear to 2.1 ± 0.4 (range 1.5 to 2.5). Although the change in mean AC/A ratio failed to reach statistical significance (t-test, $p = 0.32$) there was a reduction in the standard deviation and range of values. Mean AC/A ratio with negative lenses was 2.3 ± 1.0 (range 1.0 to 4.5) prior to lens wear and reduced slightly to 1.8 ± 0.9 (range 1 to 3), although this failed to reach statistical significance (t-test, $p = 0.30$). Mean gradient AC/A +1 ratio was unchanged with lens wear (t-test, $p = 0.56$). There was a decrease in mean gradient AC/A –1 ratio from 2.7 ± 1.0 to 1.8 ± 1.5, but this also failed to reach statistical significance (t-test, $p = 0.19$).

One patient (patient 4) had an AC/A ratio of 4.5 with plus lenses which improved to 2.5 during lens wear. Another patient (patient 5) had an AC/A ratio of 4.5 with minus lenses prior to lens wear that improved to 2.0 during lens wear. No patients showed an increase above 2.5 with either positive or negative lenses.

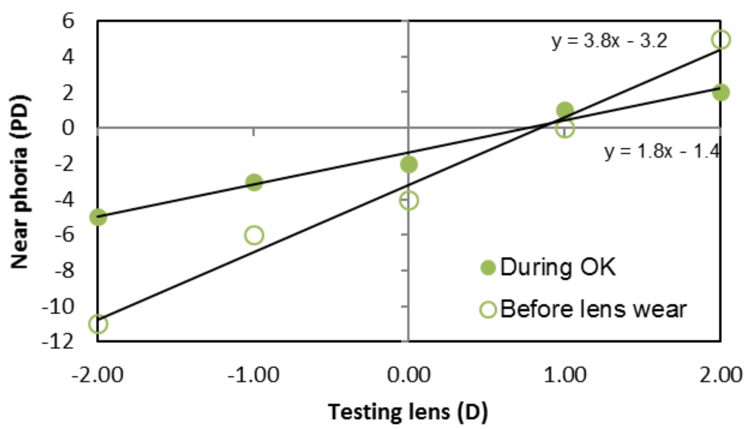

Figure 5-7 Average AC/A ratio before lens wear and during lens wear. Solid black lines are the linear regression lines. “OK” indicates orthokeratology lens wear.

5.5.2 Practice 2

Eighteen patients were used in the analysis including one patient (patient 17) with previous surgery for strabismus. Patient records received for analysis did not include age, but 17 of the 18 included the year at school or university. An approximation of mean age at commencement of lens wear was derived by adding five years to the year at school. Children in Australia begin school at kindergarten at approximately five years of age. Mean age using this approximation was 12 ± 2.9 years (range eight to 20 years). One patient had completed schooling at commencement of orthokeratology lens wear and so an estimate of age was not possible.

Mean spherical equivalent refractive error before and during lens wear is shown in Table 5-4. There was a statistically significant reduction ($p < 0.01$). These measurements were taken throughout the day with no lens wear.

	Spherical equivalent refractive error	
	Right eye	**Left eye**
	mean ± SD (range)	mean ± SD (range)
Pre-lens wear	−2.44D ± 1.12D (−0.63 to −4.50D)	−2.35D ± 1.15D (−0.75 to −4.63D)
During lens wear	+0.17D ± 0.54D (+1.25 to −0.88D)	−0.02D ± 0.87D (+0.75 to −2.88D)

Table 5-4 Mean spherical equivalent refractive (SER) error before and during orthokeratology lens wear.

Thirteen patients were corrected using BE lenses (Capricornia, Australia), four with Menicon Z CRT lenses (Menicon, Japan) and one patient had a BE lens in one eye and a Menicon Z CRT lens in the other eye.

Orthokeratology Practice 2	n	Baseline mean ± SD (range)	During treatment mean ± SD (range)	p-value
Distance phoria (Δ)	13	1.4 ± 4.6 (−4 to 11)	−0.50 ± 2.4 (−5 to 5)	0.06
Near phoria (Δ)	13	−0.5 ± 7.6 (−12 to 12)	−2.1 ± 5.7 (−10 to 9)	0.24
Lag of accommodation (D)	15	+0.77 ± 0.58 (−0.25 to +1.75)	+0.40 ± 0.56 (−0.25 to +1.50)	0.09
Positive relative accommodation (D)	17	1.72 ± 0.68 (0.75 to 3.00)	2.69 (0.75 to 3.00)	0.0001
Negative relative accommodation (D)	13	2.27 ± 0.53 (1.50 to 3.25)	1.96 ± 0.60 (0.75 to 3.00)	0.06

Table 5-5 Mean accommodation and binocular vision function before lens wear and during lens wear at Practice 2.

5.5.2.1 Distance phoria

Distance phoria was measured before and during lens wear in 13 patients. A scatter plot of individual results is found in Figure 5-8. During orthokeratology lens wear mean distance phoria shifted slightly in the exo direction but this failed to reach statistical significance (t-test, $p = 0.06$). The standard deviation of the distance phoria was lower with lens wear (F test, $p = 0.03$), and range was smaller indicating patients were closer to orthophoria with lens wear.

Of interest was that of the four patients with esophoria considered outside normal limits (2^{Δ}, 6^{Δ}, 9^{Δ} and 11^{Δ} esophoria) before lens wear, all shifted considerably closer to orthophoria during lens wear (1^{Δ} exophoria, 1^{Δ} exophoria, 3^{Δ} and 5^{Δ} esophoria respectively).

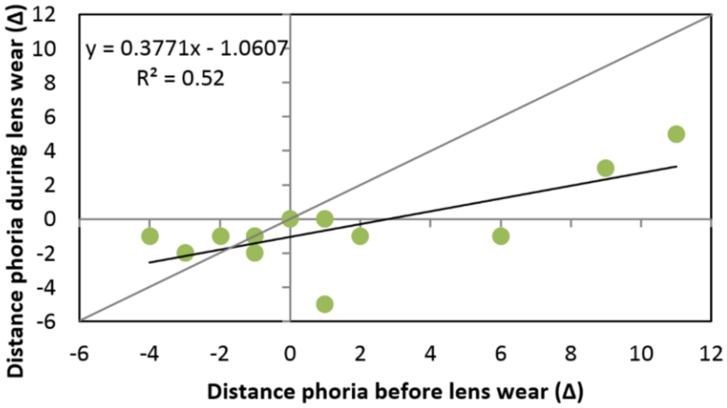

Figure 5-8 Distance phoria before lens wear compared to during lens wear in prism dioptres ($^{\Delta}$). Negative values indicate exo and positive eso. Grey line is the 1:1 line. Solid black line is the linear regression line.

5.5.2.2 Near phoria

Near phoria was measured before and during lens wear in 13 patients. A scatter plot of individual results is found in Figure 5-9. Mean near phoria was slightly shifted in the exo direction but this was not statistically significant (t-test, p = 0.24). The standard deviation was also slightly reduced but this failed to reach statistical significance (F test, p = 0.32).

Five patients had esophoria of 2^{Δ} and above prior to lens wear. These patients had a clinically and statistically significant change in phoria towards orthophoria during lens wear (t-test, p = 0.007). Four patients had near exophoria of 6^{Δ} and above prior to lens wear. Three of these patients had clinically significant changes in phoria towards orthophoria, while one increased in exophoria with lens wear. One patient had orthophoria prior to lens wear and exhibited an increase to 9^{Δ} esophoria with lens wear. This patient also indicated that vertical lines were clearer on fused cross cylinder test indicating a lead of accommodation during lens wear.

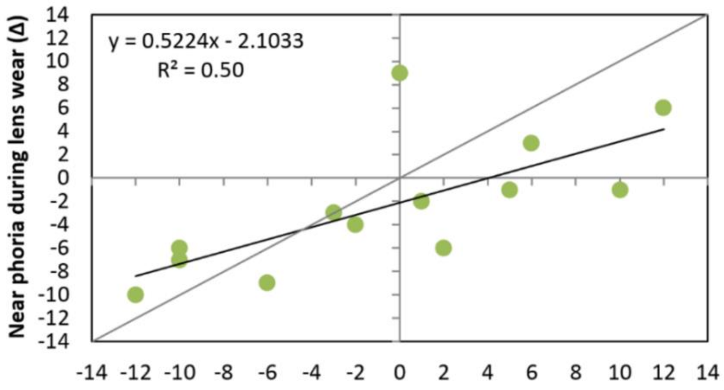

Figure 5-9 Individual near phoria before and during lens wear in prism dioptres ($^{\Delta}$). Negative values indicate exo and positive eso. Grey line is the 1:1 line. Solid black line is the linear regression line.

5.5.2.3 Lag of accommodation

A scatter plot of individual results for lag of accommodation is found in Figure 5-10. Measurements were taken on 15 patients before and during lens wear. There was on average a slight reduction of lag of accommodation during lens wear, but this failed to reach statistical significance (t-test, $p = 0.09$).

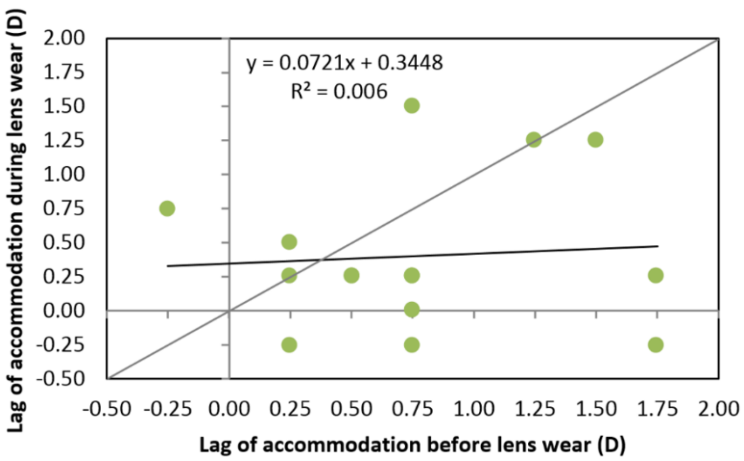

Figure 5-10 Individual lag of accommodation before and during lens wear in dioptres (D). Grey line is the 1:1 line. Solid black line is the linear regression line.

5.5.2.4 Positive and negative relative accommodation

Positive relative accommodation (PRA or B-) was measured in 17 patients. Mean positive relative accommodation improved with orthokeratology lens wear. This was a statistically significant change (t-test, $p = 0.0001$).

Negative relative accommodation (NRA or B+) was measured in 13 patients. Mean negative relative accommodation was slightly lower, although this reduction just failed to reach statistical significance (t-test, $p = 0.06$).

The range of clear vision at near improved with orthokeratology lens wear for 11 of the 13 patients. The mean improvement in range for these 11 patients was 1.09 ± 0.57D. As a group, the difference in mean range of clear vision was statistically significant (t-test, $p = 0.01$).

5.5.3 Combined data

Five of the variables of interest were measured in a similar way at the two practices. The variables were distance phoria, near phoria, lag of accommodation and positive and negative relative accommodation. Data from these variables were combined and analysed. The combined data can be found in Table 5-6. While mean distance phoria did not change during treatment with orthokeratology, there was a statistically significant decrease in the range and standard deviation (F test, $p = 0.0005$). During treatment values were closer to normal values. Mean near phoria had a statistically significant shift in the exo direction with treatment. In addition there was a reduction in the range and standard deviation of results (F test, $p = 0.01$), with values during treatment closer to normal values.

Lag of accommodation appeared to be unchanged in the combined groups cohort. Positive relative accommodation showed a statistically significant increase with treatment while mean negative relative accommodation slightly decreased. These changes were statistically significant.

Orthokeratology		Baseline	During treatment	
Combined	**n**	mean ± SD (range)	mean ± SD (range)	p-value
Distance phoria (Δ)	24	−0.2 ± 4.9 (−15 to 11)	−1.27 ± 2.3 (−5 to 5)	0.22
Near phoria (Δ)	22	−0.8 ± 6.6 (−12 to 12)	−3.3 ± 3.8 (−10 to 6)	0.01
Lag of accommodation (D)	19	+0.59 ± 0.55 (−0.25 to 1.75)	+0.43 ± 0.56 (−0.50 to 1.50)	0.21
Positive relative accommodation (D)	27	1.99 ± 0.96 (0.75 to 5.00)	2.65 ± 0.68 (1.25 to 4.00)	0.0005
Negative relative accommodation (D)	23	2.22 ± 0.52 (1.25 to 3.25)	1.91 ± 0.46 (0.75 to 2.50)	0.01

Table 5-6 Mean accommodation and binocular vision function before lens wear and during lens wear for combined data from both practices. For phoria, negative values indicate exo and positive eso.

5.6 Discussion

Mean distance phoria remained unchanged in the Practice 1 group of patients and there was a slight shift in the exo direction in the Practice 2 group, although this failed to reach statistical significance. While the mean distance phoria did not change in both groups those patients with high distance phorias (one patient with high exophoria in the Practice 1 group and four patients with high esophoria in the Practice 2 group) had clinically significant shifts towards orthophoria. In addition, the combined data showed a decreased variance in distance phorias.

Mean near phoria remained unchanged in both the Practice 1 and Practice 2 groups. However, seven of the eight patients with significant near esophoria (2^{Δ} and above) prior to lens wear had clinically significant changes towards orthophoria. Similarly, four of the five patients with significant exophoria (6^{Δ} and above) prior to lens wear exhibited clinically significant shifts in phoria towards orthophoria. Again, the combined data showed a decrease in variance with orthokeratology lens wear. There was a mean shift in phoria in the exo direction.

This improvement in phoria contrasts with other studies that have shown that near phoria becomes more convergent (eso direction) with myopia (Goss and Jackson, 1996). Also, other forms of contact lens correction have been shown to increase near phoria in an eso direction (Jimenez *et al.,* 2011).

Other studies of orthokeratology lens wear have shown a small but not statistically significant shift in near phoria in the exo direction after three months of lens wear (Brand, 2013, Felipe-Marquez *et al.,* 2016).

Lag of accommodation slightly decreased in both patient groups, although this failed to reach statistical significance. This contrasts with soft contact lens wear. Jimenez and colleagues (2011) demonstrated a clinically and statistically significant increase in lag measured with both the monocular estimate method and crossed cylinder technique with soft contact lens wear. Lag of accommodation has previously been shown to decrease following three months of orthokeratology lens wear (Tarrant, 2009, Brand, 2013).

Mean positive relative accommodation increased in both groups. This increase was statistically significant in the Practice 2 group. Mean negative relative accommodation remained unchanged in the Practice 1 group, but slightly decreased in the Practice 2 group although this failed to reach statistical significance. Overall mean range of accommodation (positive and negative relative accommodation) increased in both groups. This agrees with the results from Felipe-Marquez and colleagues (2015).

In contrast, with single vision soft contact lens correction Jimenez and colleagues (2011) found a statistically significant increase in negative relative accommodation and a slight, but not statistically significant decrease in positive relative accommodation.

In Practice 1, all patients who initially failed accommodative facility showed an improvement during orthokeratology lens wear. Orthokeratology lens wear has previously been reported to improve near accommodative facility following three months of wear (Brand, 2013). In contrast, accommodative facility reduced in soft contact lens wear (Jimenez *et al.,* 2011).

Three hypotheses are suggested here that could explain the improvement in accommodative facility with orthokeratology. First, this could simply be a practice effect. Accommodative facility has been shown to improve with re-testing (McKenzie *et al.,* 1987). McKenzie and colleagues reported a mean improvement of 4.5 cycles per minute in accommodative facility on retesting without training. This is substantially less than the mean improvement of 7.4 cycles per minute found in this cohort. Second, the improvement may be a result of the optical correction characteristics of orthokeratology lenses that act like a bifocal correction which decreases the accommodative demand at near. The third, more intriguing hypothesis relates to the association between poor accommodative facility and particularly distance accommodative facility and myopia progression (Allen and O'Leary, 2001). It is possible that an improvement in accommodative facility could be, in part, responsible for the myopia control effect seen with orthokeratology lens wear.

In this cohort, there was a slight, but not statistically significant improvement in near negative fusional reserves recovery point. The majority of patients (10 out of 12) exhibited either an unchanged or improved negative fusional reserve recovery. Again, this is in contrast with soft contact lens wear which has been shown to reduce near negative fusional reserve blur, break and recovery points (Jimenez *et al.,* 2011).

AC/A ratios were measured in six patients from Practice 1. Although this was a small sample it showed a similar result to Brand (2013) who found a decrease in AC/A ratio following three months of orthokeratology lens wear. Once again, this differs from the situation with soft contact lenses which induce no change in AC/A ratio (Jimenez *et al.*, 2011).

Overall accommodative and binocular vision function either remained unchanged or improved with orthokeratology lens wear in this cohort of patients.

Having an eso posture at near has been shown to be predictive of myopia onset (Goss, 1991, Drobe and Saint-Andre, 1995), and other research suggests near phoria that is further from orthophoria in both the eso and exo directions is associated with myopia onset (Goss and Jackson, 1996). Increased near exophoria has also been shown to be associated with small, but statistically significant increases in myopic progression. Goss and Rainey (1999) noted a relationship between higher esophoria and higher lag of accommodation in myopic children. The blur associated with a higher lag of accommodation may be a stimulus for myopia progression.

In this cohort of patients, orthokeratology lens wear appears to improve distance and near phoria in those patients who had initial phorias not close to orthophoria. It is possible that this improvement could be, in part, responsible for the myopia control effect seen with orthokeratology lens wear. A limitation of this study is that it does not include a control group. The improvement in phoria seen in this group may be the result of a practice effect or due to the repeatability of the testing method. The Von Graefe method has been shown to have an average difference between 2 trials of 1.9^{Δ} (range 0 to 5^{Δ}) (Schroeder *et al.,* 1996). However, several participants had a change in phoria significantly higher than this which is suggestive that there was an improvement of phoria with orthokeratology lens wear.

In addition, a high AC/A ratio has been associated with myopia onset (Jiang, 1995, Gwiazda *et al.,* 2005, Zadnik *et al.,* 2015) and progression (Jiang, 1995, Mutti *et al.,* 2000, Price, 2013) and is elevated in childhood myopia compared to emmetropes (Gwiazda *et al.,* 1999, Sreenivasan *et al.,* 2009). Again it is possible that the changes to AC/A ratio seen in orthokeratology lens wear may be, in part, responsible for the myopia control effect.

5.6.1 Summary of results

A summary of results from Practice 1 and Practice 2 is shown in Table 5-7. Results in agreement (highlighted in green) include the reduced range of distance phorias, no change in mean near phoria and an increase in positive relative accommodation. Accommodation and binocular vision with orthokeratology lens wear appears to either remain the same or change in a direction opposite to soft contact lens wear for measures of near phoria, positive relative accommodation, negative relative accommodation, lag of accommodation, accommodative facility, and negative fusional reserves recovery.

5.7 Conclusion

The results of this study show that orthokeratology lens wear is associated with changes in accommodation and binocular vision for some patients. Overall there was a significant decrease in the spread of distance phoria, an increase in positive relative accommodation, an improvement in accommodative facility, and possibly a reduction in AC/A ratio although this failed to reach statistical significance. There was also a slight shift in near phoria in the eso direction and decrease in lag of accommodation, although these values failed to reach statistical significance. These results contrast with conventional soft contact lens wear (Jimenez *et al.,* 2011) and represent an improvement in accommodation and binocular vision function.

These changes in accommodation and binocular vision function may in part be associated with the myopia control effect seen with orthokeratology lens wear.

	Orthokeratology Practice 1	Practice 2	Combined	Soft contact lenses Jimenez *et al.*
n	19	18	37	30
Age (years)	8 to 17	8 to 20	8 to 20	19 ± 2.4
Distance phoria	NSC	more exo (p=0.06)	NSC	NSC (p=0.07)
Variance	decrease (p<0.01)	decrease (p=0.03)	decrease (p<0.01)	
Near phoria	NSC (p=0.22)	NSC (p=0.24)	more exo (p=0.01)	more eso (p<0.05)
Variance			decrease (p=0.01)	
Positive relative accommodation	NSC (p=0.23)	increase (p=0.0001)	increase (p=0.0005)	decrease (p=0.07)
Negative relative accommodation	NSC	decrease (p=0.06)	decrease (p=0.01)	increase (p=0.01)
Lag of accommodation	NSC (p=0.68)	slight decrease (p=0.09)	NSC (p=0.21)	increase (p= 0.01)
Accommodative facility	increase (p=0.01)	x	x	decrease (p=0.06)
Distance fusional reserves	NSC	x	x	NSC
Near fusional reserves	increase NFR recovery (p=0.07)	x	x	decrease NFR break & recovery (p<0.01)
AC/A	NSC (p=0.18)	x	x	x

Table 5-7 Summary of binocular vision and accommodation findings in two Australian practices following orthokeratology lens wear compared with soft contact lens wear (Jimenez *et al*. 2011). "x" indicates outcome variable not included in report. "NSC" indicates no significant change.

5.8 Strengths and limitations

These data were obtained from "real world" clinical practice. Although they were not obtained from a controlled research environment as in Study 1, they are a better reflection of usual practice as both eyes were fitted with orthokeratology lenses.

As a retrospective review of patient records from community optometric practices this study has some limitations. Patients were not selected to meet strict criteria of patient age, and refractive error. Refractive error was measured subjectively and without cycloplegia and in some patients, was worse than ±0.50D with orthokeratology lens wear. While distance vision was good and final refractive errors were minimal in the patients included in this study, corneal topography maps were not assessed to ensure good fitting lenses.

There was variability in the time between measurements taken prior to lens wear and follow-up visits and some changes seen may have been the result of differences in accommodation and binocular vision that occur with age. Unless the time between baseline and follow-up was significant, these changes would be very small. For example, based on Hofstetter's estimation of amplitude of accommodation (Borish, 1970), the difference from age 9 to 12 years would only be 1D. Any change in phoria with age would also be small (Freier and Pickwell, 1983). Time of day of appointments was not recorded and may influence results particularly as the orthokeratology refractive effect changes throughout the day (Swarbrick, 2006).

Accommodative and binocular vision testing was not carried out on all patients and testing may not have been carried out in the same order or with similar instructions. Instructions given during accommodation and binocular vision testing can alter results (Rosenfield *et al.,* 1995, Karania and Evans, 2006). There may also be potential measurement bias from the practitioners.

From the results of this study, the importance of a sufficiently large sample size and including participants with abnormal baseline binocular vision is highlighted. A limit of this study was that there was a relatively small sample sizes in each group. However, including data from two independent practices has allowed for cross checking of results and triangulation with the data in the previous and following studies. Where appropriate, combining the data from the two practices has given the advantage of increased statistical power.

This study also highlights that only using changes in the mean result to identify changes in key accommodative and binocular vision status tests has limited value as results may move in either direction. The spread of results including standard deviation and range of values should also be considered in analysis.

Despite these limitations, similar results have been found in other similar studies of the effect of orthokeratology lenses on accommodation and binocular vision. The impact of orthokeratology lens wear on accommodation and binocular vision function warrants further investigation.

6 The impact of orthokeratology lens wear on binocular vision and accommodation 2

This chapter (Study 3) investigates the effect of short-term orthokeratology lens wear on accommodation and binocular vision function during lens wear compared to baseline in young adults. It is a prospective study.

6.1 Introduction

In the previous study, there was significant decrease in the spread of distance phoria, an increase in positive relative accommodation, and an improvement in accommodative facility during orthokeratology lens wear. There was also a slight shift in near phoria in the eso direction and decrease in lag of accommodation. The study was limited as time in lenses was variable, different lens designs were used, the quality of the lens fitting was unknown, there were varied testing instructions used to measure accommodation and binocular vision function and all tests were not completed on all patients.

Orthokeratology lens wear has previously been shown to improve near accommodative function reflected by improvements in accommodative facility, and reduction in accommodation lag and AC/A ratios (Tarrant *et al.,* 2009, Brand, 2013). Some studies have reported shifts in the exo direction in near phoria (Brand, 2013, Gifford *et al.,* 2017, Felipe-Marquez *et al.,* 2017) while other studies have demonstrated no significant changes in either distance (Felipe-Marquez *et al.,* 2017) or near phoria (McLeod, 2006). Similarly, no changes in lag of accommodation (McLeod, 2006, Felipe-Marquez *et al.,* 2015), positive and negative relative accommodation (McLeod, 2006), accommodative facility (McLeod, 2006) or monocular accommodative facility (Felipe-Marquez *et al.,*

2015) have been reported in previous studies. These studies are limited by the small sample sizes, ranges of initial binocular vision status and lens fitting criteria.

The present study sought to investigate the effects of short-term orthokeratology lens wear on accommodation and binocular visual function in a young adult population who achieved successful orthokeratology lens fitting. This study was completed in collaboration with Professor Bruce Evans, Dr Pauline Kang (UNSW), Professor Helen Swarbrick, and UNSW Optometry and Vision Science honours students, Ms Jenny Zhu and Ms Tina Chau.

6.2 Methods

6.2.1 Study design

This prospective study involved participants being fitted with orthokeratology lenses in both eyes for overnight wear. Study measurements were taken at baseline before any lens wear. They were then repeated after 28 days of overnight orthokeratology lens wear, in the morning typically within 2 hours of lens removal when maximum orthokeratology effect is expected. Only participants with successful orthokeratology lens fits, where residual refractive error was within ± 0.50 D of emmetropia, and who fulfilled the criteria described below, were included in data analysis. Accommodation and binocular vision tests were carried out at this stage without wearing any refractive over-correction.

6.2.2 Participants

This study followed the tenets of the Declaration of Helsinki and approval was obtained from UNSW, LSBU and Institute of Optometry Human Research Ethics Committees before study commencement. Twenty-four myopic adults were enrolled (age 23.2 ± 5.0 years, range 18 to 38 years). All participants gave their written consent to study participation after being informed about the nature and possible consequences of study participation. Inclusion criteria were distance spherical equivalent refractive error of

−1.00D to −4.00 D and less than or equal to 1.50DC astigmatism, no prior rigid gas-permeable contact lens wear, good ocular health and no contraindications for orthokeratology lens wear (Swarbrick, 2006).

Results from 15 participants (10 female, 5 male) are reported. Data from a further 9 participants were excluded from analysis as they did not reach one or both of the following criteria at 28 days of orthokeratology lens wear in both eyes:

- Unaided distance visual acuity of 0.1 LogMAR or better (n = 5)
- Residual spherical equivalent subjective refraction plano ± 0.50 D (n = 5, including participants who also did not fulfil visual acuity criteria).

All participants included in the analysis had well-fitting orthokeratology lenses as demonstrated by bull's eye orthokeratology topography maps (Mountford, 2004).

6.2.3 Measurements

Visual acuity: Distance LogMAR visual acuity (VA) was measured at 6 m (Test Chart Pro, Thomson Software Solutions; UK) using Sloan letters.

Central objective and subjective refraction: Non-cycloplegic central objective refraction was taken using the Shin-Nippon N-Vision K5001 autorefractor (Tokyo, Japan) and a mean of five measurements is reported. Subjective refraction was measured using standard optometric techniques (Elliot, 2007).

Corneal topography: The E300 videokeratoscope (Medmont Pty Ltd, Melbourne, Australia) was used to capture corneal topography, with data analysed using Medmont Studio 4, Version 4.12.2. An average of three maps at each visit is reported.

Binocular vision and accommodative assessment: a series of binocular function tests were administered at baseline and after 28 days of orthokeratology as described below. At baseline, measurements were taken with distance refractive error corrected with trial lenses. At the follow-up study visit, measurements were taken with orthokeratology induced emmetropia (spherical equivalent subjective refraction plano ± 0.50 D) with no over-correction in place.

- Near fixation disparity was measured using the Sheedy disparometer and Saladin near point card at 40 cm (see Appendix C0)
- Distance and near phorias were assessed with the Howell card at 3 m and 30 cm respectively (see Appendix C0)
- Gradient AC/A ratio was measured using the Howell card and +1.00D, +2.00D −1.00D and −2.00D lenses binocularly at 30 cm (see Appendix C.7.1)
- Stereopsis was tested with the Randot Stereo Test (Circles) at 40 cm (see Appendix C1.1)
- Distance and near accommodative facility was evaluated using plano/−2.00 D flippers and ±2.00D flipper lenses at 6m and 40 cm respectively (see Appendix C.6 0).

6.2.4 Contact lenses

Participants were fitted with Paragon CRT lenses (Paragon Vision Sciences, USA) in both eyes according to manufacturer guidelines. Participants were instructed on the use of orthokeratology lenses including instructions and training on lens insertion and removal, cleaning of lenses and lens case, wear regime and follow-up visits required.

6.2.5 Data and statistical analysis

Conventional sphero-cylindrical refractive error (S/C x θ) measurements were converted into power vectors to allow for statistical analysis using the following equations (Thibos *et al.,* 1997):

Spherical equivalent refraction (SER) = S + C/2

$J180 = -C\cos 2\theta / 2$

$$J45 = -C \sin 2\theta / 2$$

Stereoacuity scores were transformed to log arcsec for statistical analyses. Data were assessed for normality using the Shapiro-Wilk test. Depending on normality of data, either RM-ANOVA or Friedman test with post-hoc paired t-tests or Wilcoxon (WSR) tests were used to analyse changes in visual acuity, refraction and binocular vision. To assess changes in binocular vision measurement variability over time, two mixed models with repeated measures (compound symmetry covariance structure and a heterogeneous compound symmetry structure) and a subsequent likelihood ratio test were conducted (SPSS v.24, Chicago, USA). For this study, a critical p-value of 0.05 was used to denote statistical significance.

6.3 Results

Central objective refraction and best corrected distance visual acuity at baseline and after 28 days of orthokeratology lens wear are shown in Table 6-1.

There was a significant hyperopic spherical equivalent refraction shift after orthokeratology lens wear but no significant change in astigmatic components J180 and J45. To be included in the study residual subjective spherical equivalent refraction after 28 days of orthokeratology was within plano ± 0.50D in both eyes. There was an improvement in visual acuity after orthokeratology lens wear in both eyes. This is not a usual finding in orthokeratology lens wear and may be the result of sub-optimal correction at baseline, although the increase is not clinically significant (mean of less than half a letter chart line in right eye and less than one line in left eye). Corneal topography parameters before and after orthokeratology lens wear are shown in Table 6-2.

	Right eye				Left eye			
	SER	J_{180}	J_{45}	BCVA	SER	J_{180}	J_{45}	BCVA
Baseline	-2.09±1.21	-0.00±0.25	0.16±0.22	-0.06±0.07	-1.84±1.06	0.07±0.29	0.10±0.20	-0.05±0.08
orthokeratology	-0.17±0.63	-0.04±0.25	0.11±0.24	-0.10±0.02	-0.01±0.63	0.02±0.31	0.12±0.26	-0.13±0.23
p-value	<0.001	0.561	0.330	0.021	<0.001	0.256	0.576	0.014
	t-test	t-test	t-test	WSR	t-test	WSR	t-test	WSR

Table 6-1 Objective central refraction (D; mean ± SD), astigmatic power vectors at 180 and 45 degrees and best corrected distance visual acuity (BCVA, LogMAR units; mean ± SD) at baseline and after 28 nights of orthokeratology lens wear. “SER” indicates spherical equivalent refraction.

	Right eye			Left eye		
	r_o	Flat K	Steep K	r_o	Flat K	Steep K
Baseline	7.89 ± 0.28	42.42 ± 1.54	43.55 ± 1.46	7.87 ± 0.27	42.42 ± 1.54	43.64 ± 1.45
Orthokeratology	8.27 ± 0.36	41.09 ± 1.51	42.12 ± 1.34	8.27 ± 0.33	41.14 ± 1.57	42.32 ± 1.33
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
	t-test	t-test	t-test	t-test	t-test	t-test

Table 6-2 Apical radius of curvature r_o (mm; mean ± SD), Flat K and Steep K (D; mean ± SD) at baseline and after 28 nights of orthokeratology lens wear.

There was significant corneal flattening demonstrated by a significant increase in r_o and decrease in both Flat K and Steep K values indicating an orthokeratology lens effect.

Horizontal and vertical fixation disparity measures were completed on 12 participants with the Sheedy disparometer and 10 patients with the Saladin near point card. Vertical and horizontal fixation disparity did not change with orthokeratology when measured with both the Saladin near point card and Sheedy disparometer (all $p > 0.05$). Statistical tests used were: Sheedy horizontal, WSR; Sheedy vertical; t-test; Saladin horizontal; WSR; Saladin vertical: all values were zero so no analysis conducted) as illustrated in Figure 6-1.

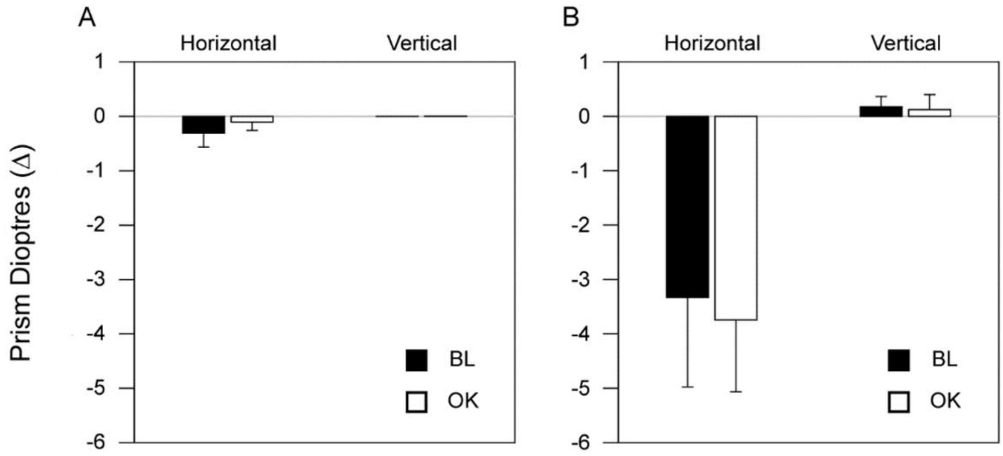

Figure 6-1 Horizontal and vertical fixation disparity at baseline (BL) and after 28 nights of orthokeratology (OK) lens wear measured with A. The Saladin near point card and B. The Sheedy disparometer. For horizontal phoria negative values indicate exo and positive eso. For vertical phoria negative values represent deviations in the right hypo direction and positive values represent deviations in the right hyper direction. Error bars represent standard error of the mean.

Prior to lens wear mean distance phoria was 0.50 ± 1.31$^{\Delta}$ exophoria (range 3$^{\Delta}$ esophoria to 2$^{\Delta}$ exophoria), as shown in Figure 6-2. After 28 nights of orthokeratology lens wear, mean distance phoria was 0.13 ± 0.74$^{\Delta}$ exophoria (range 1$^{\Delta}$ esophoria to 2$^{\Delta}$ exophoria). There was no significant change in mean distance phoria (t-test, p = 0.16) but there was a reduction in the variability (F-test, p = 0.01) and the range of values were reduced. In addition, based on the regression analysis (Figure 6-3) change in distance phoria could be estimated using the following formula: −0.60 x distance phoria + 0.06 (R^2 = 0.69; Figure 6-3). This formula indicates that in this cohort phorias close to orthophoria remained relatively unchanged, while larger baseline eso and exo phorias would move towards orthophoria to an amount approximating 0.6 of the absolute value.

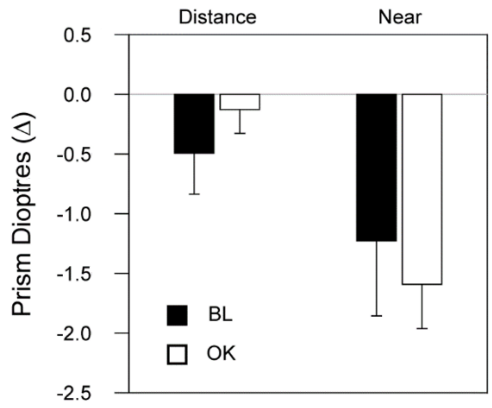

Figure 6-2 Mean horizontal distance and near phoria (prism dioptres $^{\Delta}$; mean ± SD) at baseline (BL) and after 28 nights of orthokeratology (OK) lens wear. Negative values indicate exo and positive eso. Error bars represent standard error of the mean.

Mean near phoria prior to lens wear was $1.23 \pm 2.43^{\Delta}$ exophoria (range 1^{Δ} esophoria to 8^{Δ} exophoria). After 28 nights of lens wear, mean near phoria was $1.60 \pm 1.42^{\Delta}$ exophoria (range 1^{Δ} esophoria to 4^{Δ} exophoria). There was no significant change in mean near phoria during orthokeratology lens wear (t-test, $p = 0.51$). However, there was a reduction in the variability (F test, $p = 0.02$) and the range of values was reduced. In addition, change in near phoria could be estimated using the following formula: −0.70 x near phoria −1.22 ($R^2 = 0.66$; Figure 6-3). This formula indicates that in this cohort near phorias close to orthophoria shifted slightly in the exo direction, while larger baseline eso and exophorias moved towards orthophoria to an amount approximating 0.7 of the absolute value with esophoria showing a larger shift than exophorias.

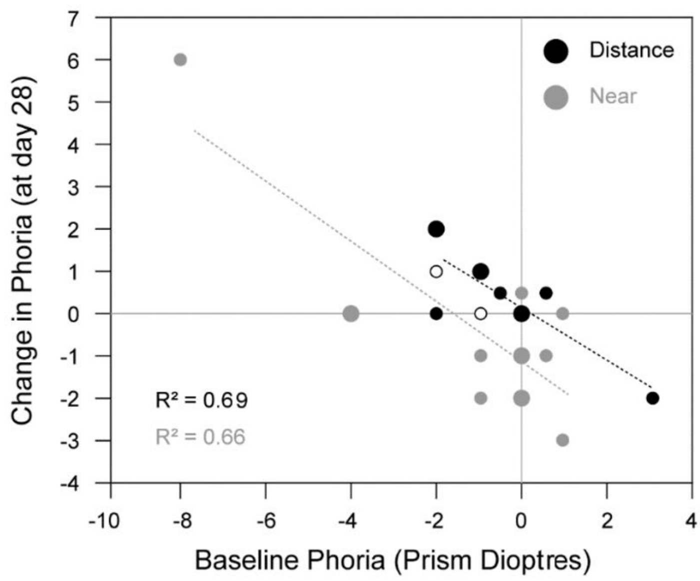

Figure 6-3 Change in distance and near phoria (prism dioptres $^{\Delta}$) after 28 nights of orthokeratology lens wear compared to distance and near phoria at baseline. Larger black and grey data points indicate overlapping distance and near data points, respectively. Black and white data points indicated overlapping distance and near data points. Negative values indicate exo and a shift in the exo direction and positive eso and a shift in the eso direction. Black dashed line is the linear regression line for distance phoria. Grey dashed line is the linear regression line for near phoria.

At baseline, stereopsis measured with distance correction was 1.39 ± 0.16 log seconds of arc or between 20 to 40 seconds of arc (range 20 to 70 seconds of arc). After 28 days of lens wear mean stereopsis was 1.34 ± 0.07 log seconds of arc or between 20 to 40 seconds of arc (range 20 to 30 seconds of arc). This change in stereopsis was not statistically significant (WSR, $p = 0.09$). However, there was a statistically significant reduction in the variance of stereo acuity scores after 28 nights of orthokeratology lens wear compared to baseline (F test, $p<0.001$). Furthermore, stereopsis was improved or was unchanged in 13 of the 15 participants.

Mean distance and near accommodative facility at baseline and after 28 nights of orthokeratology lens wear are shown in Figure 6-4. Prior to lens wear mean distance accommodative facility was 13.5 ± 5.6 cycles per minute (range 5 to 23 cycles per minute). After 28 nights of orthokeratology lens wear mean distance accommodative facility was 17.9 ± 6.4 cycles per minute (range 7 to 30 cycles per minute) although this improvement in distance accommodative facility just failed to reach statistical significance (t-test, $p = 0.053$). Mean near accommodative facility was 13.3 ± 3.3 cycles per minute (range 8 to 19 cycles per minute) at baseline and remained relatively unchanged at 14.7 ± 5.3 cycles per minute (range 1 to 22 cycles per minute) (t-test, $p = 0.25$) after 28 nights of orthokeratology lens wear.

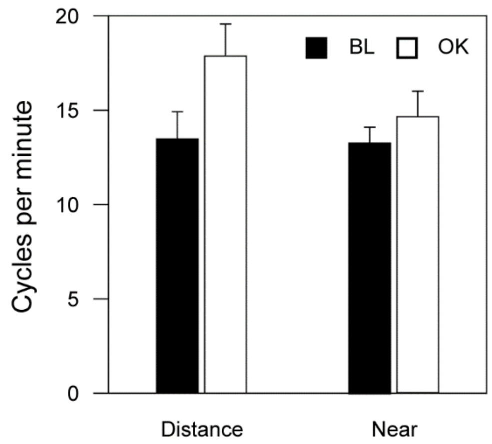

Figure 6-4 Mean distance and near accommodative facility in cycles per minute at baseline (BL) and after 28 nights of orthokeratology (OK) lens wear. Error bars represent standard error of the mean.

AC/A ratios and calculated gradient AC/A with ±1.00 D and ±2.00 D lens stimuli at baseline are shown in Figure 6-5. After 28 nights of orthokeratology lens wear, compared to baseline, there was no significant change in gradient AC/A with −2.00 D (t-test, $p = 0.65$), −1.00 D (WSR, $p = 0.19$), +1.00 D (WSR, $p = 0.41$), or +2.00 D (WSR, $p = 0.47$) lens stimuli.

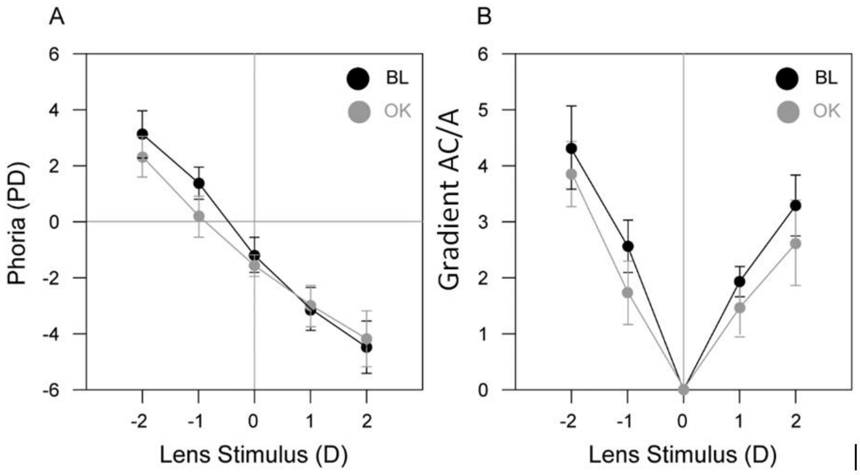

Figure 6-5 A. Mean phoria and B. gradient AC/A ratios. Gradients for ±1.00 D and ±2.00 D lens stimuli at baseline (BL) and after 28 nights of orthokeratology (OK) lens wear. Negative values indicate exo and positive eso. Error bars represent standard error of the mean.

6.4 Discussion

This study characterised accommodation and binocular vision function changes after successful short-term orthokeratology lens wear in young adult myopes. After 28 days of orthokeratology, there was significant corneal flattening, indicated by increase in r_o and decrease in Flat and Steep K values, and hyperopic shifts in spherical equivalent refraction indicating myopic correction with orthokeratology. Furthermore, there was a significant improvement in uncorrected visual acuity with orthokeratology lens wear.

Study 2 results may have been confounded by having sub-optimal fits, poor habitual acuity and significant residual refractive error. Time in lenses also varied between participants. In this Study, these limitations were controlled.

Fixation disparity is an associated measure of the misalignment of the eyes during fixation. Although a previous study demonstrated that the Saladin near point card and Sheedy disparometer yield similar measurements (Frantz *et al.,* 2011), it appears that there is a difference in horizontal fixation disparity measurements obtained using the two different methodologies in our current study. This is more consistent with the findings of

Wildsoet and Cameron (1985) who showed that there were poor relationships between results found with the Sheedy disparometer compared with other associated phoria tests. The absence of a foveal fusion lock in the Sheedy disparometer was noted as a potential reason for such poor results. Pickwell and colleagues (1988) showed that the Sheedy disparometer produced variable results compared with a Mallett unit, which he also attributed to the absence of a fusional lock with the disparometer. More recently, Alhassan and colleagues (2015) showed that the disparometer gives much more variable results than a range of other fixation disparity tests (including the Saladin card) and Alhassan and colleagues (2016) showed that the mean result of the Sheedy disparometer is very different to that with the Saladin card. However, there was no significant change in horizontal and vertical fixation disparities after orthokeratology compared to baseline using either the Saladin near point card or Sheedy disparometer.

While mean distance and near phorias did not significantly change after orthokeratology compared to baseline, there was a statistically significant reduction in the variability of both distant and near phorias where the range of data were closer to orthophoria after orthokeratology. Previous research suggests near phoria that is further from orthophoria in either the eso or exo directions is associated with myopia onset (Goss and Jackson, 1996). Additionally, increased near exophoria has also been shown to be associated with small, but statistically significant increases in myopic progression (Berntsen *et al.,* 2011). The results of our study suggest that orthokeratology lens wear reduces both distance and near phoria closer to ortho posture, which may reflect improved accommodative accuracy or function that may in turn contribute to the myopia control effects experienced with orthokeratology.

In addition, while mean stereopsis was only slightly improved, most participants showed either improved or unchanged stereopsis. The variability of stereopsis significantly reduced after orthokeratology and all subjects demonstrated stereo acuity measures between 20 to 30 seconds of arc. Of note is one participant who had reduced stereopsis at baseline (70 seconds of arc) that improved to 30 seconds of arc after 28 nights of orthokeratology lens wear coupled with improvements in near phoria (shift in eso direction towards orthophoria). Only two subjects experienced slight reduction in stereopsis (0.1 and 0.08 log seconds of arc) which was equivalent to approximately one step reduction in the Randot Stereo Test (circles) following orthokeratology lens wear. Successfully fitted orthokeratology lenses appear to have a mild positive impact on stereo acuity in most cases.

Myopes have been reported to have poor accommodative function reflected by a reduction in distance accommodative facility (O'Leary and Allen, 2001). In agreement with a previous study on the effect of orthokeratology lens wear, there was an improvement in distance accommodative facility (Brand, 2013). This is in contrast with soft contact lens wear which has been shown to worsen accommodative facility compared to single vision spectacle correction (Jimenez *et al.,* 2011). The improvement in accommodative facility after 28 nights of orthokeratology found in the current study may be the result of practice effects (McKenzie *et al.*, 1987, Allen *et al.,* 2010) or due to the nature of the multifocal optical correction achieved with orthokeratology lens wear.

This study is limited by the small sample size and few participants with accommodation and binocular vision function outside normal ranges. The study only investigated accommodation and binocular vision function in participants who achieved good vision with short-term orthokeratology lens wear. Those with poor vision, residual refractive error and poor orthokeratology lens fits were excluded from this study but may warrant further investigation. Further studies are required after longer-term orthokeratology lens wear.

This study provides further evidence that orthokeratology lens wear improves or maintains accommodative and binocular vision function in young adult myopes who achieve good vision with orthokeratology lens wear. These results suggest that myopes with distance phoria outside normal ranges, near esophoria or high exophoria and/or poor distance accommodative facility may benefit most from orthokeratology lens wear, in terms of improvement in binocular vision and accommodative posture.

7 Interactions between myopia control interventions and accommodation and binocular vision function

This chapter (Study 4) sought to investigate how accommodation and binocular vision function is altered with myopia progression control treatments. It also investigated whether initial accommodation and binocular vision function influence the efficacy of myopia control methods including orthokeratology lens wear and low dose atropine in a population of patients seen at the UNSW Myopia Clinic at the UNSW Optometry Clinic.

7.1 Background

Study 1 in this thesis suggested that initial binocular vision function may play a role in myopia progression control in orthokeratology lens wear. Studies 2 and 3 have demonstrated that orthokeratology lens wear may improve or at least maintain good accommodative and binocular vision function.

This study aimed to investigate how accommodation and binocular vision function is altered with myopia progression control treatments. It also aimed to determine if initial accommodation and binocular vision function influences the outcomes of myopia progression control treatments. This study will be limited to orthokeratology lens wear and low dose atropine treatment. It is a retrospective analysis of the clinical findings of patients presenting to the UNSW Myopia Clinic at the UNSW Optometry Clinic, UNSW (Sydney, Australia).

Prior to commencement of the study, approval was given by the UNSW Human Research Ethics Advisory Panel, and subsequently, The Institute of Optometry and LSBU approved the study by Research Ethics Committee Chair's Action.

The UNSW Myopia Clinic commenced in August 2015. The clinic accepts referrals from optometrists in New South Wales and the Australian Capital Territory, Australia as well as from the UNSW Optometry Clinic. Patients attend the clinic for baseline measurements of axial length (IOLMaster, Zeiss, Germany), subjective and objective refraction (Shin-Nippon N-Vision K5001 autorefractor, Tokyo, Japan), corneal topography (E300 Videokeratoscope, Medmont Pty Ltd, Melbourne, Australia) and binocular vision assessment using standard clinical tests. Additional history is obtained through a lifestyle questionnaire (Appendix E, p.236) and ocular health is assessed with routine optometric testing and the addition of retinal imaging with optical coherence tomography (OCT) (RS−3000 OCT Retina Scan Nikon, Japan).

Treatment options available to patients at the UNSW Myopia Clinic include low dose atropine, orthokeratology lens wear, bifocal and multifocal soft contact lenses, and bifocal and progressive addition spectacles. Following clinical measurements, options that are determined to be suitable for the patient are discussed with patients and their families to determine treatments that best suit individuals.

Patients receive an information sheet*, Lifestyle Modifications for Myopia Control* (Appendix F, p. 241) that discusses the importance of time spent outdoors and other modifications that may reduce the risk of developing myopia (Jones *et al.* 2007, Rose *et al.* 2008, Dirani *et al*. 2009, Guggenheim *et al.* 2012, Wu *et al.* 2013).

One option available to patients at the UNSW Myopia Clinic is low dose atropine. The topical application of atropine has been prescribed as a method of myopia progression control in East Asia since the early 2000s (Fang *et al.,* 2013). Over 10% of four to 18-year-old myopic children in Taiwan were prescribed the treatment in 2007. Atropine is a muscarinic receptor antagonist that inhibits the parasympathetic system. Although accommodation is controlled by the parasympathetic system, the myopia progression control effects of atropine have been shown to be through a different mechanism. This mechanism is not clearly understood (McBrien *et al.,* 1993, McBrien *et al.,* 2013). Potential mechanisms include the following hypotheses based on results from animal studies. The chick sclera has fibroblast cells with muscarinic receptors and atropine may be involved in scleral remodelling (Gallego *et al.,* 2012). In the tree shrew, retinal amacrine cells have been shown to have muscarinic receptors (Arumugam and McBrien, 2012). Atropine bound to amacrine cells may increase dopamine release and inhibit eye growth (McBrien *et al.,* 1993).

A randomised prospective controlled trial of 1% atropine use (The Atropine for the Treatment of childhood Myopia or ATOM study) showed a 77% reduction in mean myopia progression in a group of 400 children compared to children who received a drop of the vehicle solution only (Chua *et al.,* 2006). Atropine at this dose has significant visual side-effects such as light sensitivity, blur due to paralysis of accommodation and increased pupil size, the potential for retinal and lens photo-toxicity (Shih *et al.,* 1999), and the potential for systemic side-effects. Retinal function assessed by electroretinogram has been found to be unaltered in children following 2 years of atropine use (Luu *et al.,* 2005) but, longer term effects are still unknown.

A more recent randomised controlled trial of atropine at various concentrations (ATOM 2) has shown clinically significant reductions in myopia progression with treatment with a significantly lower dose of 0.01% atropine (low dose atropine) once daily (Chia *et al.*, 2012). Low dose atropine treatment has minimal visual and systemic side effects in East Asians (Chia *et al.,* 2012) and Caucasians (Loughman and Flitcroft, 2016). There is also less rebound effect following the cessation of treatment compared to higher doses (Tong *et al.,* 2009, Chia *et al*., 2012).

Low dose atropine has been shown to reduce amplitude of accommodation during treatment. Chia and colleagues (2012) reported a 2 to 3D reduction in accommodation in East Asian children on 0.01% atropine. They also noted that 7% of the participants requested reading glasses. Loughman and Flitcroft (2016) noted an 11% decrease in accommodation in 14 young adult myopes aged 18 to 27 years on 0.01% atropine in the short-term (5 days), although this was not statistically significant ($p = 0.08$). The impact of low dose atropine on other accommodation and binocular vision functions has not been reported.

7.2 Method

The records of patients from the UNSW Myopia Clinic who had parental consent for their data to be used for research and were treated with orthokeratology lens wear or low dose atropine were included in the study. Patients were excluded from the study if they had not completed an initial consultation (baseline) and a follow-up visit approximately 3 to 6 months from baseline.

The treatment modality for each patient was determined following the initial baseline measurements, assessment of suitability for each treatment and discussion with the patient and their parents.

For orthokeratology lens wear distance spherical equivalent refractive error of between −1.50 and −4.50D and less than or equal to 1.50DC corneal astigmatism were used as cut-offs. One patient was outside of this range and was only partially corrected with orthokeratology lens wear. Single vision spectacles were worn to correct the residual myopic refraction in this case. No patients had worn rigid gas permeable lenses previously. All patients had good ocular health and there were no other contraindications for orthokeratology lens wear. Patients were fitted with Paragon CRT lenses.

Baseline refractive error was not limited with low dose atropine treatment. All had good ocular health and had no contraindications for low dose atropine use including allergy.

No patients using either treatment were strabismic or amblyopic.

Patients were assigned a study number and de-identified data of interest were collated in a Microsoft Excel spreadsheet. Data included the following:

- Refractive error before and during treatment
- Objective refraction using the Shin-Nippon N-Vision K5001 autorefractor (Tokyo, Japan) performed without cycloplegia
- Distance corrected visual acuity at 6m
- Age of onset of myopia. This was then used to calculate years since diagnosis
- Age
- Type of treatment and date of commencement
- Orthokeratology lens design (where applicable)
- Axial length using the IOLMaster (Zeiss, Germany).

As the time between baseline visits and follow-up varied between patients an estimation of annual axial length change was determined using the following formula:

Annualised change in axial length = (change in axial length x 365)/ days in treatment.

Conventional sphero-cylindrical refractive error measurements were converted into spherical equivalent refraction using the following equation (Thibos *et al.*, 1997):

Spherical equivalent refraction (SER) = (Sphere (D) + Cylinder (D))/2

Accommodation and binocular vision tests included in data collection before and during orthokeratology lens wear and low dose atropine treatment were:

- Lag of accommodation at 40cm using the cross-cylinder technique (see Appendix C0)
- Distance phoria at 3m and near phoria at 33cm using the Howell card (see section Appendix C0)

- Near accommodative facility with ±2.00D flipper lenses and a working distance of 40cm for 1 minute (see section Appendix C.6)
- Stereopsis with the Randot Stereo Test Mark 1 at 40cm (see Appendix C.9 1.1)
- Gradient AC/A ratio at near (33cm) using +1.00D, +2.00D, −1.00D and −2.00D spherical lenses (see Appendix C.7.1)
- Negative and positive relative accommodation at near using N8 test type at 40cm. First blur was taken as the endpoint (see Appendix C.5 0)
- Distance (6m) and near fusional reserves (40cm) using Risley prisms (see Appendix C.3 0).

In Study 1 participants were grouped according to their response to orthokeratology and rigid gas permeable lens treatment for comparison. Due to the small sample size in this study, a similar approach to analysis for orthokeratology lens wear was not feasible. Baseline variables of interest were directly compared to change in annualised axial length as a proxy measure for myopia progression.

For patients treated with low dose atropine the sample size in the present study was larger and an approach similar to Study 1 was used. Patients were grouped according to annualised axial length growth of 0.10mm per year and under as ‘Atropine strong responders’ (n = 10) or those above 0.10mm per year as ‘Atropine non-responders’ (n = 8). The cut-off of 0.10mm per year was based on the results of previous studies that have reported that children who remain emmetropic have an average annual rate of axial length progression of 0.10mm (Mutti *et al.,* 2007).

Individual accommodation and binocular vision variables of interest were graphed to compare before lens wear to during lens wear. Microsoft Excel was used to determine lines of best fit and coefficient of determination (R^2), and correlations (R) were determined using SPSS. For changes in accommodation and binocular vision function with orthokeratology and low dose atropine treatment, data were tested for normality using the Shapiro-Wilks test. Variables were then analysed using post-hoc t-tests or Wilcoxon (WSR) test as appropriate. Variance (standard deviation) of data was analysed using the F Test, calculated with Microsoft Excel. A p-value of <0.05 was taken to denote statistical significance.

7.3 Results

7.3.1 Orthokeratology

7.3.1.1 Orthokeratology baseline characteristics

A total of nine patients treated with orthokeratology had baseline and follow-up data from a period between approximately three to six months available. There were three males and six females. Seven (78%) were born in Australia with one patient born in China and one patient where country of birth was unknown. Ethnicity was reported as Caucasian for one (11%), East Asian for three (33%), Asian for two (22%) and two of mixed race (22%). One patient’s ethnicity was not recorded. Baseline refractive error, axial length, binocular vision and accommodation data are shown in Table 7-1.

Mean time in treatment for the cohort ($n = 9$) was 203 ± 56 days and ranged from 119 to 252 days. For investigating associations between baseline accommodation and binocular vision function and annualised axial length growth, results for the right eye only were used for analysis as mean refractive error and axial length were highly correlated between the two eyes ($R = 0.96$, $p<0.001$ and $R = 0.98$, $p = 0.02$ respectively). There was also no statistically significant interocular difference in the mean values (t-test, $p = 1.0$ and t-test, $p = 0.89$ respectively). Mean annualised change in axial length in the right eye was −0.08 ± 0.17 mm (range −0.23 to 0.26 mm).

Baseline	n	Orthokeratology mean ± SD (range)
Age (years)	9	12.6 ± 1.8 (9.5 to 14.8)
Years since diagnosis	9	3.3 ± 2.7 (1.2 to 9.7)
Right eye SER (D)*	9	−3.78 ± 1.77 (−2.00 to −7.88)
Left eye SER (D)*	9	−3.78 ± 1.98 (−1.50 to −8.00)
Right eye axial length (mm)	9	24.96 ± 1.01 (23.45 to 27.01)
Left eye axial length (mm)	9	24.97 ± 1.03 (23.52 to 27.14)
Accommodation and binocular vision function	**n**	mean ± SD (range)
Distance phoria (Δ)	8	−0.6 ± 1.0 (−2 to 1)
Near phoria (Δ)	9	−0.4 ± 1.6 (−3 to 1)
Lag of accommodation (D)	9	+0.06 ± 0.66 (−0.75 to +1.50)
Accommodative facility (±2.00D) (CPM)	9	7.7 ± 5.2 (0 to 14.5)
Gradient AC/A +1	9	1.9 ± 0.7 (1 to 3)
Gradient AC/A −1	9	2.9 ± 3.4 (0 to 10)
Stereopsis (log seconds of arc)	9	1.56 ± 0.21 (1.3 to 1.8)

Table 7-1 Baseline data for orthokeratology patients. For phoria, negative values indicate exo and positive eso. “SER” indicates spherical equivalent refraction. *3 patients’ baseline SER M was taken from subjective refraction.

7.3.1.2 Change in accommodation and binocular vision function with orthokeratology lens wear

As this was a review of clinical records, some of the data were missing from either baseline or subsequent testing. Results were compared when baseline and follow-up data were available.

Orthokeratology	n	Baseline mean ± SD (range)	During treatment mean ± SD (range)	p-value
Distance phoria (Δ)	7	−0.5 ± 1.0 (−2 to 1)	−0.4± 1.1 (−2 to 1)	0.90
Near phoria (Δ)	8	−0.3 ± 1.6 (−3 to 1)	−1.6 ± 1.8 (−4 to 0.5)	0.002
Lag of accommodation (D)	8	+0.06 ± 0.70 (−0.75 to 1.50)	+0.09 ± 0.42 (−0.50 to 0.75)	0.26
Accommodative facility (±2.00D) (CPM)	6	7.7 ± 4.7 (0 to 14)	5.6 ± 3.1 (0 to 8.2)	0.80
Gradient AC/A +1	8	1.9 ± 0.8 (1 to 3)	1.1 ± 1.3 (0 to 4)	0.11
Gradient AC/A −1	8	3.0 ± 3.6 (0 to 10)	2.1 ± 1.4 (0.5 to 5)	0.35
Stereopsis (log seconds of arc)	5	1.63 ± 0.20 (1.30 to 1.85)	1.48 ± 0.16 (1.30 to 1.60)	0.35

Table 7-2 Accommodation and binocular vision function before and during orthokeratology lens wear. For phoria, negative values indicate exo and positive eso.

In this study, there was a statistically significant shift in mean near phoria in the exo direction (t-test, p = 0.002). All patients either had a shift in phoria in the exo direction or remained unchanged. A scatter plot of individual results is given in Figure 7-1.

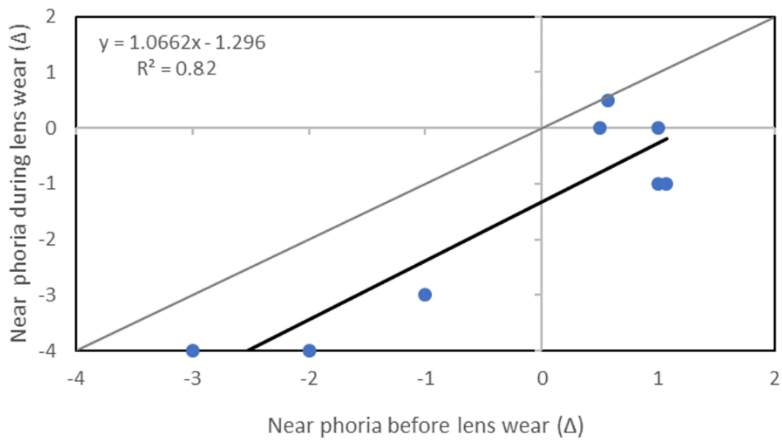

Figure 7-1 Scatter plot of near phoria before orthokeratology lens wear and during lens wear in prism dioptres (Δ). Negative values indicate exo and positive eso. Grey line indicates 1:1 line. Solid black line is the linear regression line.

While there was a slight decrease in gradient AC/A +1 ratio with orthokeratology lens wear, this failed to reach statistical significance (t-test, p = 0.11). All other accommodation and binocular vision test mean results remained unchanged. However, there was a statistically significant decrease in the variance of the gradient AC/A −1 ratio (F test, p = 0.03) indicating more patients attained normal gradient AC/A ratios with orthokeratology lens wear. A scatter plot of individual results is given in Figure 7-2. The two patients who had very high ratios prior to lens wear (7 and 10 respectively) exhibited the greatest change in gradient AC/A 1 ratio. They also had the greatest annualised axial length growth of the cohort.

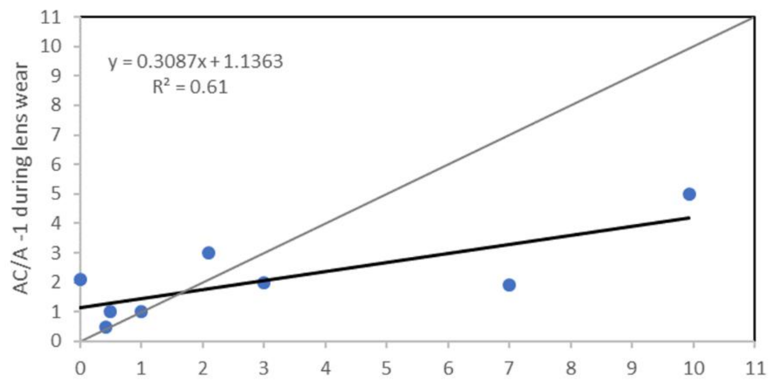

Figure 7-2 Gradient AC/A −1 before and during orthokeratology lens wear. Grey line is the 1:1 line. Black line is the linear regression line.

7.3.1.3 Orthokeratology myopia progression

Annualised change in axial length was correlated against baseline demographic, accommodation and binocular vision function variables to analyse any trends in response to treatment. Correlations comparing change in axial length to baseline characteristics are summarised in Table 7-3.

There was a low correlation between age and change in axial length with older patients showing less axial length growth but this failed to reach statistical significance (correlation (R) = 0.39, p = 0.30). Age, years since diagnosis, initial spherical equivalent refractive error, and baseline axial length were not correlated with change in axial length.

Baseline gradient AC/A −1 was moderately correlated with change in axial length (correlation (R) = 0.74, p = 0.01), with patients with higher AC/A −1 ratio having greater annualised axial length growth. The gradient AC/A +1 ratio was moderately correlated with change in axial length (correlation (R) = 0.66), and this reached borderline statistical significance (p = 0.05). Patients with lower gradient AC/A +1 ratio had greater annualised axial length growth, which was opposite to the gradient AC/A +1 ratio. A scatter plot of individual results can be found in Figure 7-3 and Figure 7-4.

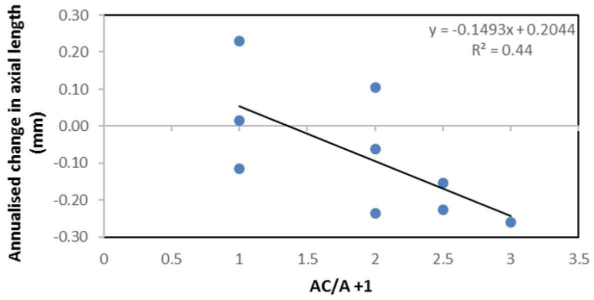

Figure 7-3 Relationship between baseline gradient AC/A +1 and annualised axial length change in orthokeratology lens wear. Black line indicates linear regression line.

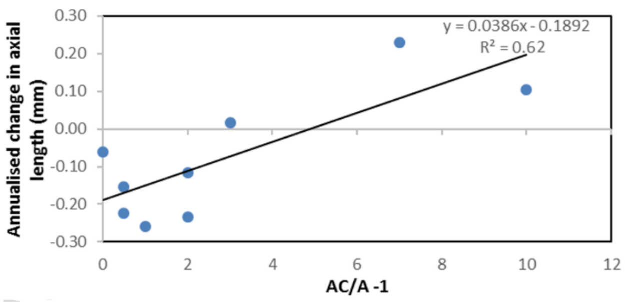

Figure 7-4 Relationship between baseline gradient AC/A −1 and annualised axial length change in orthokeratology lens wear. Black line indicates linear regression line.

Stereopsis was positively correlated with change in axial length (correlation (R) = 0.72, p = 0.03), indicating that people with worse stereopsis were less likely to respond to myopia control with orthokeratology. A scatter plot of individual results can be found in Figure 7-5.

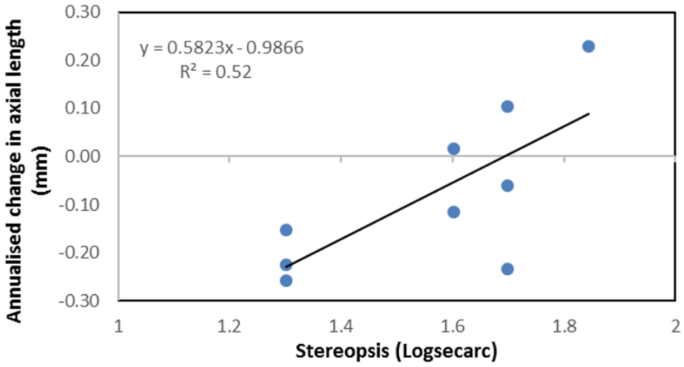

Figure 7-5 Relationship between baseline stereopsis and annualised axial length change in orthokeratology lens wear. Black line indicates the linear regression line.

Distance phoria, near phoria, lag of accommodation and accommodative facility were not linearly correlated with annualised change in axial length in this group of patients.

Correlations with annualised change in axial length		
	Orthokeratology (correlation)	
	R	p value
Age	0.39	0.30
Years since diagnosis	−0.27	0.48
Right eye SER	0.13	0.74
Axial length (right eye)	0.06	0.88
Distance phoria	0.26	0.53
Near phoria	−0.30	0.44
Lag of accommodation	−0.11	0.78
Accommodative facility (± 2.00D)	0.32	0.40
Gradient AC/A +1	0.66	0.05
Gradient AC/A −1	0.74	0.01
Stereopsis	0.72	0.03

Table 7-3 Correlation analysis of the relationship between baseline demographic and baseline accommodation and binocular vision function variables and annualised change in axial length.

7.3.2 Low dose atropine

7.3.2.1 Low dose atropine baseline characteristics

A total of 18 patients treated with low dose (0.01%) atropine had baseline and three to six-month data available. There were 7 males and 11 females. Fourteen (78%) were born in Australia with one patient born in each of the following countries; Japan, Singapore, UK and the USA. Ethnicity was reported as Caucasian for nine (50%), East Asian for six (33%), Asian for two (11%) and one of mixed race (East Asian/Caucasian) (6%). Baseline refractive error, axial length, binocular vision and accommodation data are found in Table 7-4. Mean time in treatment for this cohort (n = 18) was 151 ± 62 days and ranged from 79 to 324 days. For analysis of change in accommodation and binocular vision, participants were included when both baseline and follow-up results were available for each variable. For investigating associations between baseline accommodation and binocular vision function and annualised axial length growth, results for the right eye only were used as mean refractive error and axial length were highly correlated between the two eyes (correlation (R) = 0.96, $p < 0.001$ and correlation (R) = 0.97, $p < 0.001$ respectively) and there were no statistically significant interocular differences in the mean values t-test, $p = 0.72$ and t-test, $p = 0.56$ respectively). Mean annualised change in axial length in this group was 0.19 ± 0.27 mm (range −0.09 to 0.97mm). A graph with each participant's individual annualised axial length change can be found in Figure 8-1.

		Low dose atropine
Baseline	**n**	mean ± SD (range)
Age (years)	18	11.6 ± 2.0 (6.0 to 14.0)
Years since diagnosis	18	3.4 ± 2.4 (0 to 8.5)
Right eye SER (D)	18	−3.96 ± 2.04 (−1.00 to −7.50)
Left eye SER (D)	18	−4.01 ± 2.17 (−0.50 to −8.00)
Right eye axial length (mm)	18	25.01 ± 1.02 (22.95 to 27.51)
Left eye axial length (mm)	18	25.05 ± 1.06 (22.92 to 27.63)
Accommodation and binocular vision function	**n**	mean ± SD (range)
Distance phoria (Δ)	18	−1.0 ± 1.8 (−6 to 2)
Near phoria (Δ)	18	−1.6 ± 2.8 (−6 to 2)
Lag of accommodation (D)	17	+0.15 ± 0.67 (−1.75 to +1.25)
Accommodative facility (±2.00D) CPM	17	8.7 ± 2.7 (4 to 13)
Gradient AC/A +1	18	2.1 ± 1.8 (0 to 6)
Gradient AC/A −1	18	2.5 ± 1.4 (0 to 5)
Stereopsis (log seconds of arc)	17	1.60 ± 0.25 (1.30 to 2.15)
Amplitude of accommodation (D)	13	13.2 ± 2.5 (7.7 to 16.7)

Table 7-4 Baseline data for low dose atropine patients. For phoria, negative values indicate exo and positive eso. “SER” indicates spherical equivalent refraction.

7.3.2.2 Changes in accommodation and binocular vision function with low dose atropine

Means and standard deviations of accommodation and binocular vision function tests at baseline and during treatment can be found in Table 7-5.

Low dose atropine		Baseline	During treatment	
	n	mean ± SD (range)	mean ± SD (range)	p-value
Distance phoria (ᐞ)	10	−1.4 ± 2.0 (−6 to 1)	−1.5 ± 1.4 (−5 to 0)	0.80
Near phoria (ᐞ)	10	−1.8 ± 2.9 (−6 to 2)	−3.5 ± 4.2 (−15 to 0)	0.27
Lag of accommodation (D)	14	+0.23 ± 0.50 (−0.50 to 1.25)	+0.09 ± 0.33 (−0.25 to 0.75)	0.27
Accommodative facility (±2.00D) (CPM)	5	8.7 ± 3.0 (4 to 12)	9.3 ± 1.9 (8 to 12)	0.65
Gradient AC/A +1	9	1.8 ± 1.0 (0 to 3)	1.7 ± 1.5 (0 to 5)	0.82
Gradient AC/A −1	9	2.6 ± 1.8 (0 to 5)	2.3 ± 1.9 (0 to 6)	0.74
Amplitude of accommodation (D)	10	13.5 ± 2.6 (7.8 to 16.7)	12.2 ± 2.8 (9.1 to 16.7)	0.19

Table 7-5 Change in accommodative and binocular vision function with low dose atropine.

Mean amplitude of accommodation decreased very slightly with low dose atropine use, however the reduction failed to reach statistical significance (t-test, p = 0.19).

There was a trend for mean near phoria to shift in the exo direction with treatment (t-test, p = 0.27). One patient had a large, clinically significant increase of 12 ᐞ in near phoria in the exo direction with low dose atropine use. For a scatter plot of individual responses see Figure 7-6.

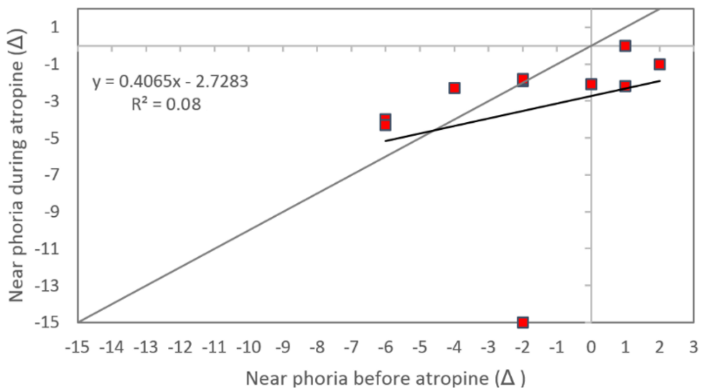

Figure 7-6 Individual near phoria (ᐞ) before low dose atropine compared to during treatment with low dose atropine. Grey line is the 1:1 line. Black line is the linear regression line.

While there was no statistically significant change in mean gradient AC/A −1 or gradient AC/A +1 ratios, two patients had large increases in gradient AC/A −1 with treatment.

A scatter plot of individual gradient AC/A −1 ratios is shown in Figure 7-7.

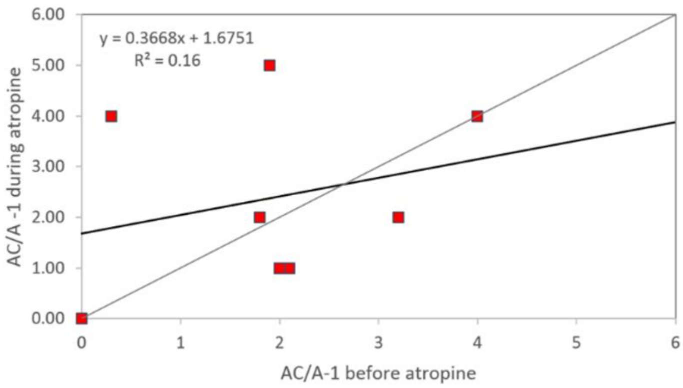

Figure 7-7 Individual gradient AC/A −1 ratio before low dose atropine compared to during treatment with low dose atropine. Grey line is the 1:1 line. Black line is the linear regression line.

All other accommodation and binocular vision functions tested remained unchanged including mean distance phoria, lag of accommodation and stereopsis.

7.3.2.3 Low dose atropine myopia progression

Baseline mean amplitude of accommodation was higher in the ‘strong responders’ compared to the ‘non-responders’ group (t-test, $p = 0.02$). ‘Strong responders’ had a slightly lower baseline gradient AC/A+1, although this just failed to reach statistical significance (t-test, $p = 0.06$). In addition, the variance of gradient AC/A +1 was lower in the ‘strong responders’ compared to the ‘non responders’ group (F test, $p = 0.01$). While mean lag of accommodation was not statistically significantly different between the two groups there was a trend to increased variance in results (F test, $p = 0.10$).

	Atropine strong responders mean ± SD (range)	Atropine non-responders mean ± SD (range)	p value
n	10	8	
Age (years)	11.5 ± 1.3 (6.0 to 14.0)	11.6 ± 2.5 (10.0 to 13.3)	0.97
Annualised change in axial length (mm)	−0.02 ± 0.08 (−0.09 to 0.10)	0.39 ± 0.28 (0.13 to 0.97)	<0.001
Initial axial length (mm)	25.21 ± 1.31 (22.95 to 27.51)	24.79 ± 0.66 (23.74 to 25.74)	0.40
Right eye SER (D)	−4.49 ± 2.15 (−1.50 to −7.50)	−3.75 ± 1.77 (−1.13 to −6.50)	0.69
Years since diagnosis	4.6 ± 2.3 (2.0 to 8.5)	2.9 ± 1.9 (0.7 to 5.1)	0.28
Distance phoria ($^{\Delta}$)	−1.3 ± 2.2 (−6 to 2)	−0.8 ± 1.3 (−2 to 1)	0.75
Near phoria ($^{\Delta}$)	−2.3 ± 2.1 (−6 to 2)	−1.3 ± 3.3 (−6 to 2)	0.64
Gradient AC/A +1	1.3 ± 0.9 (0 to 3)	3.0 ± 2.3 (0 to 6)	0.06
Gradient AC/A −1	3.1 ± 1.4 (1 to 5)	2.1 ± 1.3 (0 to 4)	0.23
Lag of accommodation (D)	0.28 ± 0.46 (−0.50 to 0.75)	0.00 ± 0.87 (−1.75 to 1.25)	0.41
Accommodative facility (CPM)	8.5 ± 3.0 (4 to 13)	9.4 ± 2. 2 (6.5 to 12)	0.36
Stereopsis (log seconds arc)	1.67 ± 0.24 (1.3 to 2.15)	1.51 ± 0.26 (1.3 to 2.0)	0.28
Amplitude of accommodation (D)	14.5 ±1.7 (12.5 to 16.7)	11.3 ± 2.5 (7.7 to 14.3)	0.02

Table 7-6 Baseline binocular vision characteristics in patients treated with low dose atropine grouped into those showing the greatest myopic progression (non-responders) and those showing the least myopic progression (responders) For near phoria, negative values indicate exo and positive eso. “SER” indicates spherical equivalent refraction.

7.3.2.4 Additional analyses

There was no statistically significant correlation between annualised change in axial length and years since diagnosis, age, spherical equivalent refractive error and axial length Table 7-7.

Correlation annualised change in axial length		
	Low dose atropine (correlation)	
	R	p value
Age	−0.19	0.44
Years since diagnosis	−0.42	0.07
SER (right eye)	0.18	0.46
Axial length (right eye)	−0.21	0.39
Distance phoria	0.21	0.40
Near phoria	0.28	0.24
Lag of accommodation	0.05	0.84
Accommodative facility (± 2.00D)	0.19	0.44
Gradient AC/A +1	0.15	0.53
Gradient AC/A −1	−0.28	0.24
Stereopsis	−0.14	0.58
Amplitude of accommodation	0.34	0.24

Table 7-7 Correlation analysis of the relationship between baseline characteristics and annualised axial length growth with low dose atropine treatment. “SER” indicates spherical equivalent refraction.

No baseline accommodation and binocular vision function tests correlated with annualised change in axial length. In contrast to the group comparisons, there was no correlation between baseline amplitude of accommodation and annualised change in axial length. A scatter plot of amplitude of accommodation and change in annualised axial length change can be found in Figure 7-8.

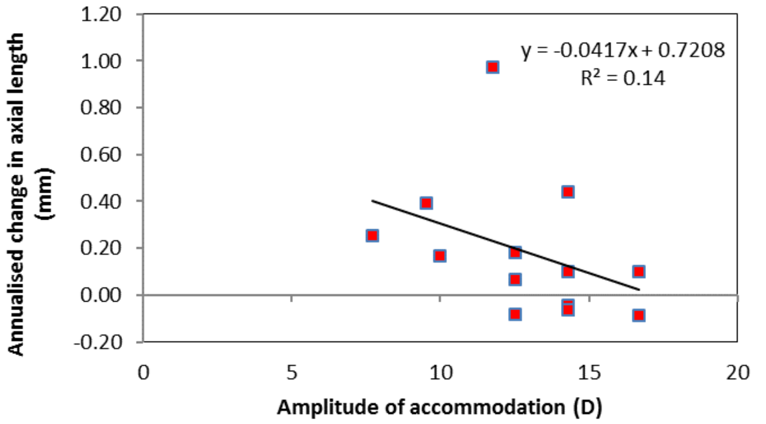

Figure 7-8 Baseline amplitude of accommodation compared with annualised change in axial length. Black line is the linear regression line.

7.3.3 Comparison between groups

Baseline characteristics of the orthokeratology lens wearing group and the low dose atropine group were compared. Data were tested for normality using the Shapiro-Wilks test. Variables were then analysed using post-hoc t-tests or Wilcoxon (WSR) test as appropriate. There were no statistically significant differences in mean baseline characteristics of age, years since diagnosis, axial length or refractive error between the orthokeratology and low dose atropine patients. All mean accommodation and binocular vision function tests were also not statistically significantly different in the two groups (Table 7-8).

Baseline	Correlation p-value
Age (years)	0.15
Years since diagnosis	0.83
SER right eye	0.77
SER left eye	0.74
Axial length right eye	0.81
Axial length left eye	0.77
Distance phoria	0.54
Near phoria	0.31
Lag of accommodation	0.72
Accommodative facility (±2.00D)	0.50
Gradient AC/A +1	0.76
Gradient AC/A −1	0.57
Stereopsis	0.67

Table 7-8 Comparison of baseline characteristics and accommodation and binocular vision function between orthokeratology and low dose atropine groups. "SER" indicates spherical equivalent refraction.

7.4 Discussion

This study characterised accommodation and binocular vision function changes with orthokeratology lens wear or low dose atropine treatment in a group of myopic children over approximately 3 to 6 months.

7.4.1.1 Changes to accommodation and binocular vision function with orthokeratology

In the orthokeratology group, there were significant hyperopic shifts in spherical equivalent refraction and changes to corneal curvature indicating myopic correction with orthokeratology.

Mean distance phoria did not significantly change from baseline. However, there was a statistically significant shift in the exo direction in near phoria. In this study there was no statistically significant change in the standard deviation for both distance and near phoria. This is in contrast to Study 2 and 3. This may be in part due to the initial smaller range of distance and near phorias in this study and distance and near phorias closer to normal. It may also be in part due to differences in accommodative response from children to young adults or due to the relatively short treatment period in Study 3.

Mean stereopsis was unchanged with orthokeratology lens wear although 4 out of 5 patients exhibited improvement. One patient had mildly reduced stereopsis at baseline of 70 seconds of arc and improved to 20 seconds of arc. This was accompanied by an improvement in gradient AC/A −1 from 7 to 2. One patient had slightly reduced stereopsis with orthokeratology lens wear from 20 seconds of arc to 40 seconds of arc, but this is unlikely to be clinically significant.

Mean accommodative facility was unchanged in this group. Four out of six patients had improved or unchanged accommodative facility with lens wear. Two patients had reduced accommodative facility with orthokeratology lens wear. One patient was only partially corrected and required spectacle wear in addition to their orthokeratology correction. Improvements in accommodative facility may be the result of practice effects (McKenzie *et al.,* 1987) or due to the nature of the multifocal correction achieved with orthokeratology lens wear.

Mean gradient AC/A +1 and mean gradient AC/A −1 were slightly reduced in this study. While this failed to reach statistical significance, 2 patients had clinically significant reductions in AC/A −1 ratios closer to normal ranges with lens wear.

7.4.1.2 Orthokeratology and myopia progression

The sample size for this study was small and treatment period was short so caution should be taken in the interpretation of the results.

The baseline variables of refractive error, age, initial axial length and years since diagnosis all were not statistically significantly different from the low dose atropine group. From a clinical perspective, it is interesting to note that there do not seem to be any differences in the sub-groups who choose orthokeratology and low dose atropine for myopia control interventions. For the research, this has the advantage of supporting a comparison of the two groups in other respects since the groups seem to be closely matched.

Axial length growth in myopes has been found to be greatest in the years just prior to and following onset (Mutti *et al.,* 2007) with decreasing growth over time. However, in this cohort, annualised change in axial length was not correlated with years since diagnosis. This may indicate improved myopia progression control treatment effect in those closest to diagnosis. Additional investigation is warranted.

In contrast to Study 1, baseline axial length did not appear to be predictive of axial length growth in this cohort.

Gradient AC/A +1 and gradient AC/A −1 were both correlated with axial length growth. Patients with a gradient AC/A +1 of 2 to 3 had a mean annualised axial length growth lower than those with a lower AC/A ratio. Those with gradient AC/A −1 of 2 had a mean annualised axial length growth lower than those with higher ratios. High AC/A ratios are associated with myopia onset (Jiang *et al.,* 1995, Gwiazda *et al.,* 2005, Zadnik *et al.,* 2015) and progression (Jiang, 1995, Price *et al.,* 2013). Orthokeratology lens wear reduced the gradient AC/A −1 ratio which may in part be associated with the treatment effect.

Stereopsis was positively correlated with annualised axial length growth with poorer initial stereopsis associated with greater growth (not responding well to myopia progression control with orthokeratology lens wear). This again is in contrast with the low dose atropine group. Poor stereopsis is associated with poor accommodation and binocular vision function (Evans, 2007) and this may have contributed to more eye growth. A correlation between myopic astigmatism and anisometropia, and stereopsis was found in a group of children in Taiwan (Yang *et al.,* 2013) with greater amounts of astigmatism and anisometropia associated with poorer stereopsis.

7.4.1.3 Limitations

This part of the study is limited by the small sample size, short period of treatment and few patients with baseline accommodation and binocular vision function outside of the normal ranges. Any influence of accommodation and binocular vision function on myopia progression control may be more obvious with participants that have worse baseline data.

7.4.1.4 Changes to accommodation and binocular vision function with low dose atropine.

There was a small decrease in mean amplitude of accommodation with low dose atropine treatment although this failed to reach statistical significance (t-test, p = 0.19). This is consistent with findings from previous studies in Asian (Chia *et al*., 2012) and Caucasian populations (Loughman and Flitcroft, 2016). It is important to note that this reduction in accommodation with low dose atropine is so slight (less than 1.50 D) that it is clinically as well as statistically insignificant. Indeed, other accommodative variables (mean lag and accommodative facility) actually improved marginally (non-significantly) with low dose atropine. This agrees with the literature suggesting that atropine 0.01% has minimal side-effects and the extension of this finding to a mostly Caucasian population in the present study will be reassuring to many practitioners in the West.

Due to the close relationship between accommodation and convergence the slight change in amplitude of accommodation seen in this study may be responsible for the changes seen in other accommodative and convergence function tests. There was a small shift in the mean near phoria towards the exo direction. Three patients who were originally esophoric at near prior to low dose atropine treatment had small shifts in the exo direction with low dose atropine treatment and no longer had esophoria at near. A phoria that is outside the normal ranges has been found to be a risk factor in myopia (Goss and Jackson, 1996). Bifocal and progressive addition lenses are thought to exhibit a myopia progression control effect as they decrease lag of accommodation and esophoria at near (Aller, 2014).

In contrast, one patient showed a significant increase in phoria in the exo direction at near. At baseline this patient had significant exophoria at distance and poor stereopsis indicating poor accommodation and binocular function that appeared to be worsened with low dose atropine use.

Mean gradient AC/A -1 slightly increased with low dose atropine use (t-test, $p = 0.06$). Two patients had significant increases in AC/A -1 ratio. Three remained unchanged while three had a slight decrease. From this study, there appears to be unpredictable changes in AC/A-1 ratios with low dose atropine use. Mean accommodative facility and lag of accommodation appeared unchanged.

These findings suggest that accommodative and binocular vision function may alter minimally with low dose atropine use. Although the treatment effects of low dose atropine are from a different mechanism to the anti-muscarinic effect of normal dose atropine (McBrien *et al.,* 1993), slight changes in accommodation and binocular vision function may impact on the treatment effect. Further investigation of the effect of low dose atropine particularly in those patients with phoria in the eso direction prior to treatment appears warranted.

Patients who exhibit poor baseline accommodative and binocular vision function should be closely monitored to ensure that adequate function continues throughout treatment. Optical interventions such as bifocal spectacles may be required to ensure maintenance of comfortable, clear vision.

7.4.1.5 Low dose atropine and myopia progression

In this cohort, annualised change in axial length was not correlated with years since diagnosis. Axial length growth in myopes has been found to be greatest in the years just prior to and following onset (Mutti *et al.,* 2007), with decreasing growth over time.

There was a statistically significant difference in baseline amplitude of accommodation with the low dose atropine ‘strong responders’ having mean amplitude of accommodation higher than the low dose atropine ‘non-responders’. A review of individual patients’ accommodation and binocular vision function before and during treatment did not give any clear reason for this association. However, it could be speculated that high amplitude of accommodation may be the result of a slightly overactive accommodative system. Low dose atropine may dampen the accommodative response slightly and alter the close relationship between accommodation and convergence to improve overall function. An alternate hypothesis is that poor initial amplitude of accommodation which is then made worse by treatment could lead to an overall worsening of the accommodation and binocular vision function decreasing its myopia progression control.

While myopes have been reported as having lower amplitude of accommodation than emmetropes, amplitude of accommodation was not found to be predictive of myopia progression (Allen and O’Leary, 2006).

The low dose atropine ‘non-responders’ group had a slightly higher mean gradient AC/A +1 ratio which just failed to reach statistical significance with a statistically significant larger variance compared to the low dose atropine ‘strong responders’. In addition, there was a trend toward greater variance in lag of accommodation in the ‘non-responders’ group (t-test, $p = 0.10$). These findings suggest that accommodation and binocular vision function that is outside normal ranges prior to treatment may lead to poorer myopia progression control with treatment. Alternatively, it may be that those patients with abnormal accommodation and binocular vision function prior to treatment may have faster progressing myopia, and while treatment may have slowed eye growth, the levels were still above normal values for this age group (Goss and Jackson, 1996, Gwiazda *et al.,* 2005, Allen and O'Leary, 2006, Price *et al*., 2013).

7.4.1.6 Limitations

This study is limited by the small sample size short treatment time, a small number of patients with poor baseline accommodation and binocular vision function and lack of a control group. Another potential limitation was the use of an approximated annualised axial length increase based on a shorter time frame. This may have introduced some error. For example one patient treated with low dose atropine showed significant axial length growth in the time period in one eye, the other eye receiving the same treatment with less treatment. There was less axial length growth in this patient at subsequent visits.

Test results were carried out my multiple practitioners which may have introduced inter-examiner variations in results and decreasing the reliability of the results. An attempt to minimize this was made by ensuring standardised testing methods by each practitioner.

7.5 Conclusions

This chapter has reviewed the first cohort of patients in a new university myopia clinic. The interactions between baseline accommodation and binocular vision variables and myopia progression control, and the change in accommodation and binocular vision variables after a few months of myopia progression control have been evaluated.

Accommodation and binocular vision function appears to be improved or unchanged with orthokeratology lens wear for most patients. While the results of this study should be taken with caution due to the small sample size, improvements in accommodation and binocular vision function may be associated with the myopia progression control treatment effect.

Low dose atropine may slightly alter the accommodation and binocular vision function of patients. For some patients, for example those with near esophoria, the change may be beneficial and may improve the treatment effects. However, for some patients the accommodative and binocular vision function may be adversely affected and supplementary treatments should be used to ensure clear and comfortable vision. Patients on myopia progression control treatment with low dose atropine, particularly those with initial poor amplitude of accommodation, should be monitored closely as they may be at risk for greater axial length growth.

8 General discussion and conclusions

This work has investigated the impact of orthokeratology lens wear and low dose atropine on accommodation and binocular vision function. It has also investigated if accommodation and binocular vision function prior to myopia control interventions, including orthokeratology and low dose atropine, has any association with the efficacy of treatment.

This thesis investigated 2 research questions:

1. Possible associations between baseline accommodation and binocular vision function and the efficacy of myopia progression control treatments was investigated with two studies:
    - Study 1: Review and re-analysis of data from a previously completed randomised controlled trial of orthokeratology lens wear
    - Study 4: A retrospective review of clinical records of children seen in a university optometric clinic.
2. The impact of orthokeratology on accommodation and binocular vision function was assessed in three studies:
    - Study 2: A retrospective review of clinical records of myopic children and young adults seen in 2 private practices
    - Study 3: A short-term prospective study of myopic young adults
    - Study 4: A retrospective review of clinical records of children seen in a university optometric clinic.

In addition, the final study (Study 4) investigated the impact of low dose atropine on accommodation and binocular vision function.

8.1 Change in accommodation and binocular vision function with myopia progression control treatment

8.1.1 Orthokeratology

Study 2, 3 and 4 have found that accommodation and binocular vision function appear to either remain unchanged or move in a direction of improved function with orthokeratology lens wear. This has not been previously reported and is a novel finding of this thesis. A summary of the changes to mean values and variability of results can be found in Table 8-1.

Throughout the studies there was either no change in mean values of accommodation and binocular vision function or an improvement. Additionally, there was either no change in variation of data or there was improvement. This provides further evidence that orthokeratology lens wear improves or maintains accommodation and binocular vision function with short to medium term lens wear in a variety of settings and across a wide age range. This result is in contrast to soft contact lens wear which has been shown to negatively impact on accommodation and binocular vision function (Jimenez *et al.,* 2011).

Of note, while mean distance phoria remained unchanged, there was a decrease in variation of results in most studies. This decrease in variation represents more participants with distance phoria closer to ortho (or normal values) with orthokeratology lens wear. Study 4 did not show any change in variation of distance phoria, but this is most likely due to the small sample size and smaller initial range of distance phorias which were also within normal ranges.

Table 8-1

	Orthokeratology Practice 1	Practice 2	Combined	Study 3	Study 4
n	19	18	37	15	9
Age (years)	8 to 17	8 to 20	8 to 20	18 to 38	9 to 15
Distance phoria	NSC	more exo (p=0.06)	NSC	NSC	NSC
variance	decrease (p<0.01)	decrease (p=0.03)	decrease (p<0.01)	decrease (p=0.01)	NSC
Near phoria	NSC	NSC	more exo (p=0.01)	NSC	more exo (p<0.01)
variance	x	x	decrease (p=0.01)	decrease (p=0.02)	NSC
Positive relative accommodation	increase (p=0.23)	increase (p<0.01)	increase (p<0.01)	x	x
Negative relative accommodation	NSC	decrease (p=0.06)	decrease (p=0.01)	x	x
Lag of accommodation	NSC	decrease (p=0.09)	NSC	x	NSC
Accommodative facility	increase (n) (p=0.01)	x	x	increase (d) (p=0.05)	NSC (n)
Distance fusional reserves	NSC	x	x	x	x
Near fusional reserves	increase* (p=0.07)	x	x	x	x
Gradient AC/A	NSC	x	x	NSC	NSC (p=0.11) +1
variance	x	x	x	x	decrease (p=0.03) −1
Fixation disparity	x	x	x	NSC	x
Stereopsis	x	x	x	NSC	NSC
variance	x	x	x	decrease (p<0.01)	x
Amplitude of accommodation	x	x	x	x	x

Mean near phoria appears to move in an exo direction with orthokeratology lens wear. Again there is a relatively consistent finding across the studies of reduction in variation of results with more participants with near phoria closer to the normal range with orthokeratology lens wear.

Brand (2013) found a slight, but not statistically significant change in phoria in the exo direction with lens wear in a small cohort. Gifford and colleagues (2016) found more exophoria at near with orthokeratology lens wear compared to soft contact lens wear but did not report a change in phoria with orthokeratology lens wear. Soft contact lens wear has been associated with changes in phoria in the eso direction (Jimenez *et al.*, 2013).

Lag of accommodation appeared to be unchanged with orthokeratology lens wear across all studies. This is in contrast with Tarrant and colleagues (2009) who found that lag of accommodation decreased with orthokeratology lens wear and Gifford and colleagues (2016) who found a lower lag of accommodation in orthokeratology lens wear compared to soft contact lens wear. These differences could be attributed to the measurement methods used, the study design and the participants' age. Tarrant and colleagues (2009) measured spherical aberrations and calculated lag of accommodation from these results in young adults. Gifford and colleagues (2016) used the monocular estimate method to measure lag of accommodation and found higher mean values than in any of the studies in this thesis. The monocular estimates method may be less accurate when viewing through the corneal changes of central corneal flattening and mid-peripheral steepening (Swarbrick 2006) associated with orthokeratology lens wear. In addition, the results were compared to soft contact lens wearers. Soft contact lens wearers have been found to have greater lag of accommodation than a control group of spectacle lens wearers (Jimenez *et al.,* 2013).

It is difficult to determine if the changes in binocular vision and accommodation with orthokeratology lens wear are due to actual improvements in accommodative and vergence functions, or due to the multifocal properties of the cornea. Central corneal flattening and mid-peripheral corneal steepening are the typical corneal topographic changes induced by myopic orthokeratology lenses (Swarbrick, 2006). The mid-peripheral corneal steepening inadvertently creates a ring of plus power relative to central corneal refractive power (Kang and Swarbrick, 2013) which in turn is hypothesised to create a relative positive retinal defocus, or a near add (Kang and Swarbrick, 2011, Kang and Swarbrick, 2016,). Thus, the mild changes in accommodation and vergence that were reported in these studies may be due to participants using the peripheral near addition correction.

A novel finding in this thesis is the improvement (reduction) in the variance or range of the results for many measures of accommodation and binocular vision. This has not been reported previously in the literature. In this thesis, comparison of the variance or range of the results, individual participant responses as well as comparing means gave further insight into the impact of treatments on accommodation and binocular vision function. Comparing variance or range is particularly important with comparing distance and near phoria where shifts away from or towards zero in either direction can be indicative of change but may not be evident when comparing means only, with exophoria scored as negative numbers and esophoria as positive numbers.

This thesis also highlights the importance of the participant’s initial accommodation and binocular vision function. The reduction in variance or range of results was more obvious when participants’ initial values were larger and outside normal ranges.

8.1.2 Low dose atropine

Low dose atropine did not significantly alter mean accommodation and binocular vision function results of distance phoria, near phoria, lag of accommodation, accommodative facility, gradient AC/A ratio and amplitude of accommodation. Previous studies have reported small decreases in amplitude of accommodation with low dose atropine use

(Chia *et al.,* 2012, Loughman and Flitcroft, 2016). In the study reported in this thesis, there was a slight decrease in mean amplitude of accommodation but this failed to reach statistical significance (t-test, $p = 0.19$). This may be due to the small sample size, younger age group and the time in treatment used in the study. Loughman and Flitcroft (2016) found the reduction in amplitude of accommodation in the first five days of treatment in young adults, and this may decrease with longer time in treatment.

Of note is that some individual participants had changes in accommodation and binocular vision results with low dose atropine use. All patients with initial near esophoria had changes in phoria in the exo direction (closer to normal) with treatment. In addition one patient had significant increased exophoria with treatment. It is inferred from these results that while the group did not change significantly, accommodation and binocular vision should be monitored in individual patients throughout treatment.

8.2 Impact of baseline accommodation and binocular vision function on myopia progression control treatment

A graph of the participants' individual annualised axial length growth for Study 1 (orthokeratology and rigid gas permeable lens wearing eyes shown separately) and Study 4 is shown in Figure 8-1. This graph highlights the individual variation in response to myopia progression control treatments.

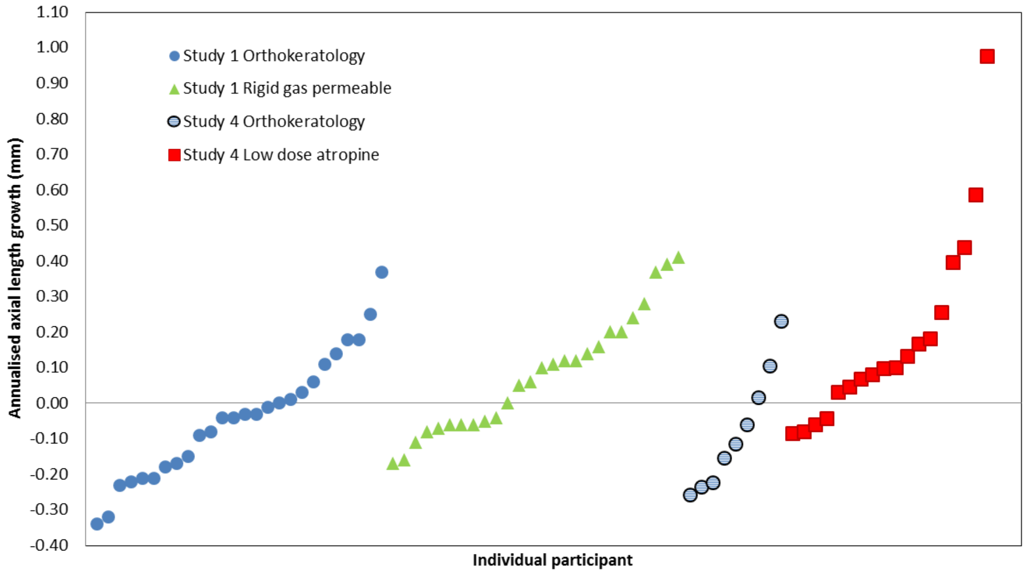

Figure 8-1 A graph of participants' individual annualised change in axial length in Studies 1 and 4.

A summary of the impact of baseline accommodation and binocular vision function on myopia control results from Studies 1 and 4 can be found in Table 8-2.

8.2.1 Orthokeratology

Study 1 suggested that the baseline accommodation and binocular vision characteristics of lag of accommodation, accommodative facility and gradient AC/A ratio may influence myopia progression control in orthokeratology lens wear. Accommodation and binocular vision function that was closer to normal was associated with less axial length growth.

In Study 4, although limited by small sample size, there was a statistically significant correlation between gradient AC/A ratio (for both +1 and -1) and axial length increase. Higher gradient AC/A -1 and lower gradient AC/A +1 being associated with increased axial length growth. There was also a correlation between stereopsis and axial length increase with poorer stereopsis showing increased growth. There was no apparent correlation with lag of accommodation or accommodative facility. This is a novel finding of this study which has not been previously reported.

The finding of an association of axial length growth with initial AC/A ratio and not lag of accommodation is in contrast to the use of bifocals or progressive addition lenses for myopia control. Bifocal or progressive addition spectacles have been reported to have greater treatment effect when patients exhibit esophoria at near (Goss and Grosvenor, 1990, Fulk *et al.,* 2000, Hasabe *et al.,* 2008), high lag of accommodation (Hasabe *et al.,* 2008, COMET 2, 2011) and a combination of esophoria at near and increased lag of accommodation (Gwiazda *et al.,* 2004, COMET 2, 2011).

The differences in axial length growth may be attributed to improved treatment effect with certain accommodation and binocular vision function characteristics prior to orthokeratology lens wear. However, the differences may also be a result of abnormal binocular vision being associated with myopia onset and progression. For a full review see section 2.3.

Table 8-2

	Orthokeratology		Atropine		RGP
	Study 1 responders v non-responders	**Study 4** correlation	**Study 4** responders v non-responders	**Study 4** correlation	**Study 4** responders v non-responders
Distance phoria	no difference	no correlation	no difference	no correlation	no difference
Near phoria	no difference	no correlation	no difference	no correlation	closer to normal (exo in non-responders)
Lag of accommodation	closer to normal in responders	no correlation	no difference	no correlation	no difference
Accommodative facility	higher in responders	no correlation	no difference	no correlation	no difference
Gradient AC/A	closer to normal in responders	correlation	+1 closer to normal in responders	no correlation	higher
variance	x	x	lower in responders	x	x
Stereopsis	no difference	correlation	no difference	no correlation	no difference
Amplitude of accommodation	x	x	higher in responders	no correlation	x
Positive relative accommodation	no difference	x	x	x	higher
Negative relative accommodation	no difference	x	x	x	lower

Summary of findings from studies investigating possible associations between baseline accommodation and binocular vision function and myopia treatment effect. "x" indicates not assessed in that study.

Studies 2, 3 and 4 have shown that with orthokeratology lens wear accommodation and binocular vision function either remained unchanged or improved with treatment. This is a novel finding of this thesis which has not been previously reported. The exact role of near phoria posture in myopia development and progression is not well understood and the innate cross-interactions between accommodation and phoria creates further difficulties in understanding the role. Changing accommodation with the use of lenses can also influence phoria postures; positive lenses to reduce accommodation (Cheng *et al.,* 2008) will cause shifts in phoria in the exo direction (Jiang *et al.,* 2007) while negative lenses induce shifts in the eso direction at near. Goss and Rainey (1999) noted a relationship between higher esophoria and higher lag of accommodation in myopic children and previous studies have suggested that having eso posture at near can be predictive of myopia onset (Goss, 1991, Drobe and de-Saint-Andre, 1995).

Previous studies exploring myopia control with other modalities such as progressive addition spectacle lenses (Gwiazda *et al.,* 1993) and centre distance bifocal soft contact lenses (Aller *et al.,* 2016) have provided evidence that individuals with poor accommodative or binocular vision function such as high lags of accommodation or near esophorias at baseline may achieve better myopia control effects. It is possible that improvement in accommodative facility, distance and near phoria and stereopsis seen with orthokeratology lens wear could be, in part, responsible for the myopia control effect. Future studies (see section 8.4) are required to determine the influence of baseline binocular vision posture on the efficacy of myopia control with orthokeratology.

8.2.2 Low dose atropine

Similar to orthokeratology lens wear, there appeared to be a greater treatment response when the baseline accommodation and binocular vision functions are closer to normal. In this cohort, gradient AC/A −1 and amplitude of accommodation were closer to normal in the patients who responded best to low dose atropine, although there were no statistically significant correlations with these tests and axial length growth. This is a novel finding of this thesis. Further investigation of this possible association appears warranted.

The results of Study 4 of this thesis, although limited by the small sample size in each cohort, sheds some light on the possible associations of accommodation and binocular vision function on myopia treatment effects. Close monitoring of accommodation and binocular vision function is warranted in both orthokeratology and low dose atropine use.

8.3 Strengths and limitations

This thesis has used a combination of real clinical samples and more classical experimental designs. The use of real clinical samples helps make the results more relevant to clinicians. Having a combination of different study populations with similar results adds to the strengths of the findings.

One of the limitations of the studies in this thesis is the difficulty of determining if the changes in accommodation and binocular vision function are due to the multifocal properties of the cornea with orthokeratology lens wear. Changes in accommodation and binocular vision function on cessation of orthokeratology lens wear may shed some light on this issue. However, the time it takes for the cornea to resume its pre-treatment shape (Swarbrick, 2006) would make it difficult to determine changes accurately. Alternatively, it may be possible to assess changes in accommodation and binocular vision with bifocal contact lens wear and cessation of wear. Potential confounders to the results also include the use of various orthokeratology lens designs. Lens design has been shown to influence accommodation and binocular vision function in studies conducted in Spain (Felipe-Marquez *et al.,* 2015, Felipe-Marquez *et al.,* 2017). However, the similarity of results found between the studies of this thesis infer that the differences between lens designs may be small.

Other factors have been found to be associated with myopia onset and progression. These include genetic factors, daylight exposure, visual hygiene, near work and pupil size (for a review of other factors associated with myopia onset and progression see Flitcroft, 2012). These factors were not controlled throughout the studies and may be potential confounders of the results.

8.3.1 Statistical Power

8.3.1.1 Change in accommodation and binocular vision with treatment

The finding of no statistically significant change in mean values of some of the accommodation and binocular vision function results throughout this thesis may indicate that there was no meaningful change with treatment, or this could be a spurious finding owing to low statistical power attributable to the modest sample size. This issue was addressed by calculating the minimum change from baseline that the study would have been able to detect as statistically significant (using the calculator at www.biomath) for key variables used throughout this thesis. This program was also used to provide estimated sample sizes for future studies where appropriate.

Four key variables will be discussed below. They have been chosen as they may have been expected to change with orthokeratology treatment (distance phoria, lag of accommodation and AC/A ratio) or low dose atropine treatment (amplitude of accommodation) based on previous published studies and apparent trends in results in this study that just failed to reach statistical significance.

8.3.1.1.1 Distance phoria

The combined data of study 2 had the greatest power for detecting change in distance phoria. The calculated minimum change the study could detect was 2.1 $^{\Delta}$ (α = 0.05 and Power = 0.80). It is possible that the change in mean distance phoria was smaller than this value. However, a modest change in mean distance phoria may have less clinical significance than the finding that distance phorias tend to move toward more normal values with treatment as demonstrated by a reduction in variance. In any event, 2Δ is less than the typical test-retest repeatability of horizontal phoria (Casillas and Rosenfield, 2006), so a smaller change than this is unlikely to be clinically significant.

8.3.1.1.2 Lag of accommodation

The combined data of study 2 had the greatest power for detecting change in lag of accommodation. The calculated minimum change the study could detect was 0.38D (α = 0.05 and Power = 0.80) which is similar to the interexaminer reliability of MEM retinoscopy of 0.31D (Goss *et al.,* 2005). However, it must be acknowledged that the change in mean lag of accommodation was smaller than this value. Gifford and colleagues (2017) found a 0.31D lower mean lag of accommodation in orthokeratology wearers compared to soft contact lens wearers. Further investigation of this variable with a sample size estimated at 20 participants is warranted.

8.3.1.1.3 AC/A ratio

Throughout this thesis mean AC/A ratio was not significantly changed. However, the power of the study that was greatest for detecting change was 1.4. This is potentially larger than clinically significant but smaller than the repeatability of the test which has been reported to be between 1.20 and 2.22 (Escalante and Rosenfield 2006). Further investigation of this variable with an estimated sample size (estimated at 21) is also warranted.

8.3.1.1.4 Amplitude of accommodation

In previous studies of low dose atropine use, amplitude of accommodation was reduced with treatment (Chia *et al.,* 2012, Loughman and Flitcroft, 2016). While mean amplitude of accommodation was decreased in Study 4 of this thesis, this failed to reach statistical significance. The calculated minimum change the study could detect was 2.90D (α =

0.05 and Power = 0.80). Further investigation with a larger sample size (estimated to be 42) is warranted as reported changes in amplitude of accommodation are approximately 10% (or 1.50D). However, considering that for the ages considered in this thesis, the minimum to maximum ranges are typically 2-2.5D based on the Hofstetter formula, it seems likely that even with the modest samples sizes in this thesis, clinically significant changes would have been detected.

8.3.1.2 The possible impact of baseline accommodation and binocular vision on efficacy of treatment

The finding of no statistically significant influence of accommodation and binocular vision function on myopia progression control may indicate that there was no meaningful association, or again, this could be a spurious finding owing to low statistical power attributable to the modest sample size. This issue was addressed by calculating the difference in mean values that the study would have been able to detect as statistically significant (using the calculator at www.biomath). This program was also used to provide estimated sample sizes for future studies where appropriate.

AC/A ratio was found to possibly influence treatment efficacy in low dose atropine but this just failed to reach statistical significance (t-test p = 0.60). In orthokeratology lens wear no influence was found (t-test, p = 0.10). For orthokeratology lens wear the calculated minimum difference the study could detect was 1.6 (α = 0.05 and Power = 0.80) but smaller than the repeatability of the test which has been reported to be between 1.20 and 2.22 (Escalante and Rosenfield 2006). The difference may be smaller than this, while still being clinically significant. Based on these results a larger sample of 28 is suggested.

The studies have identified the importance of including participants with a wide range of accommodation and binocular vision function as this can significantly alter results. In addition, the use of means only to analyse results has been shown to be limited. No change in mean may be accompanied by reductions or increases in range of results that may be clinically significant.

Throughout this thesis, participant's individual results have also been analysed to look for trends or interesting findings. This has added depth of understanding to the results that may have been lost by looking at grouped results only.

8.4 Future studies

This thesis has suggested some interesting associations between accommodation and binocular vision function in myopia progression. Continued evaluation of the role of accommodation and binocular vision on the treatment effect particularly in relation to variables that become closer to population norms with lens wear would be of value. In addition, further investigation of possible changes in accommodation and binocular vision function in those patients with baseline values outside of normal ranges deserves further investigation.

9 References

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Appendix A Acronyms and symbols

Δ	prism dioptre
%	percentage
AC/A	accommodative convergence to accommodation ratio
ATOM	Atropine for the Treatment Of childhood Myopia
BF	bifocal (spectacles)
BL	baseline
cm	centimetres
CI	confidence interval
CL	contact lens
CPM	cycles per minute
CRT	Corneal Reshaping Therapy (lens)
D	dioptre
K	keratometry
LORIC	Longitudinal Orthokeratology Research In Children
LSBU	London South Bank University
m	metres
MCOS	Myopia Control with Orthokeratology contact lenses in Spain
NFR	negative fusional reserves
NRA	negative relative accommodation
NSC	no significant change
OK	orthokeratology
PAL	progressive addition lens spectacles

PCI	partial coherence interferometry
PFR	positive fusional reserves
PRA	positive relative accommodation
ROK	Research in OrthoKeratology (Group)
R	correlation coefficient
R^2	coefficient of determination
RGP	rigid gas permeable (contact lens material)
ROMIO	Retardation Of Myopia In Orthokeratology
SEM	standard error of the mean
SER	spherical equivalent refraction
SD	standard deviation
SOP	esophoria at near
SMART	Stabilizing Myopia by Accelerating Reshaping Technique
SPSS	Statistical Package for the Social Sciences
RCT	randomised controlled trial
UNSW	University of New South Wales (Sydney, Australia)
WSR	Wilcoxon Signed Rank

Appendix B Glossary of terms

Accommodation	Adjustment of the shape of the lens to change the focus of the eye. When the ciliary muscle is relaxed, suspensory ligaments attached to the ciliary body and holding the lens in position are stretched, which causes the lens to be flattened. The eye is then able to focus on distant objects. To focus the eye on near objects the ciliary muscles contract and the tension in the ligaments is thus lowered, allowing the lens to become rounder. Adjustments in convergence also contribute to accommodation.
Astigmatism	Defect of vision in which the image of an object is distorted because not all the light rays come to a focus on the retina. Some parts of the object may be in focus but light from other parts may be focused in front of or behind the retina. This is usually due to irregular curvature of the cornea and/or lens, whose surface resembles part of the surface of an egg (rather than a sphere). The defect can be corrected by wearing cylindrical lenses, which produce exactly the opposite degree of distortion and thus cancel out the distortion caused by the eye itself. (Oxford Concise Medical Dictionary 2017).
Hypermetropia	The condition in which parallel light rays are brought to a focus behind the retina when the accommodation is relaxed. Moderate degrees of hypermetropia may not cause blurred vision in children and young adults because of their ability to accommodate, but for older people and those with greater degrees of hypermetropia near vision is more blurred than distance vision. Normal vision can be restored by wearing spectacles with convex lenses. (Oxford Concise Medical Dictionary 2017).

Myopia	The condition in which parallel light rays are brought to a focus in front of the retina. Closer objects are clearer as compared to distant objects. Myopia is corrected by wearing spectacles with concave lenses; contact lenses and surgery can also be used to correct myopia (Oxford Concise Medical Dictionary, 2017).
Optometrist	Primary healthcare practitioners of the eye and visual system who provide comprehensive eye and vision care, which includes refraction and dispensing, the detection/diagnosis and management of diseases in the eye, and the rehabilitation of conditions of the visual system. (Definition from the World Council of Optometry).
Orthokeratology	The use of specially designed rigid gas permeable lenses to temporarily reshape the cornea to correct ametropia.
Phoropter	"A phoropter is one of several generic names for modern instruments containing an optometer (battery of lenses for determination of optical error), combined with prisms and other attachments for measuring binocularity. The term refractor is another such term, and "vision tester" or other descriptive terms are used because phoroptor, spelled with "-or", is actually a trademark of one company" ("*Visual Optics and Refraction*" by David D. Michaels, Mosby 1980, p. 232).
Binocular vision	"Binocular vision is the coordination and integration of what is received from the two eyes separately into a single binocular percept" (Evans, 2007).

Appendix C Accommodation and binocular vision function tests

The accommodation and binocular vision function response to orthokeratology lens wear warrants further investigation. In addition, the influence of accommodation and binocular vision function on the myopia progression control of myopia progression control treatments should be assessed. If certain binocular vision functions are associated with greater treatment effects, treatments could be better tailored to individuals.

C.1 Distance and near heterophoria

For comfortable distance vision, the visual axes of the eyes should be parallel to each other. If there is an imbalance in the extraocular muscles controlling eye alignment, then when one of the eyes is covered it will drift away from a parallel position. The movement may be horizontal, vertical or cyclo-rotational. If the movement is horizontal it will either be in towards the nose (eso movement) or away from the nose (exo movement). The amount of movement (phoria) can be measured in a variety of ways as discussed below.

The simple cover-uncover test described above is one form of dissociation test and heterophoria can be measured with any test that dissociates the eyes by presenting different images (non-fusible images) to each eye. Methods to produce dissociation consist of excluding the view of one eye from the other (the cover test, Maddox Wing), distorting the image of one eye (Maddox Rod test, Modified Thorington), and displacing the images with prism (Von Graefe, Prentice/Howell Phoria Chart).

Phoria can be measured at any distance, but typically at distance (6m) and near (commonly 40cm). For distance phoria the head is in a position so that the eyes are in the primary position (that is, looking straight ahead). The refractive correction (if any) that is worn should be specified.

Typically, a distance of 40cm is used for near testing, although some tests (for example the Howell Phoria Chart) are designed to be used at a distance of 33cm. In the clinical setting, it is most relevant to test phoria at the habitual distance(s) that the patients use for near tasks. The targets used in the test should control accommodation for the testing distance by using a sufficiently detailed test target. In the clinical setting, it is most relevant to use a target that ideally simulates the type of near work material used by the patient.

C.1.1 Cover test

The cover test is often described as an objective test because the practitioner makes a judgement of the results rather than the patient. It is used to determine misalignment of the eyes and whether a deviation is a phoria or has decompensated and is strabismic. It also allows the practitioner to estimate the magnitude of the deviation and, in phoria, the recovery. The cover test can assess eye alignment in all directions of gaze. Therefore, it is useful in the diagnosis of individual extra-ocular muscle palsies which impact on eye alignment differently in different directions of gaze. The test is performed in free space and can be carried out even if a patient is suppressing the images from one eye, for example in long standing strabismus. It can also be carried out on very young children and infants.

The cover test is first performed with the eyes in the primary position and the refractive correction, if any, should be specified. Care must be taken to discover whether the current spectacle prescription includes any compensating prism as this will influence the results. Patients are asked to focus on a letter on a letter chart at 6m. While observing one eye the other eye is covered with an occluder. If the uncovered eye deviates, then a strabismus is present. Eye movement of the uncovered eye in towards the nose indicates exotropia and out indicates esotropia. If no movement is noted in the uncovered eye the occluder is removed from the covered eye and the observer checks for movement in this eye. Any movement indicates phoria with movement towards the nose indicating exophoria and away from the nose indicating esophoria.

Estimates of the size of movement can be used to evaluate the size of the deviation in prism dioptres. Alternatively, the movement can be neutralised with prism lenses to determine the size of the deviation. The cover test can also be repeated at near with a near target. A great deal of information can be obtained from a cover test and a fuller description of the several varieties of the cover test (for example, the alternating cover test) can be found in Evans (2007).

C.1.2 Von Graefe (Borish, 1970, Evans, 2007)

The Von Graefe test is usually performed through a phoropter. Patients wear any appropriate refractive correction and view a single letter close to the limits of resolution. The eyes are dissociated using base up prism (usually 6^{Δ}) in one eye so that the patient sees two images vertically displaced. Horizontal prism is introduced in front of the other eye and moved until the images align vertically. The horizontal prism is moved from the opposite direction to again align the images and the average of these two readings is taken as the deviation (Borish, 1970). Images can also be dissociated horizontally to determine vertical phoria. Results are measured in prism dioptres. Phorias that are corrected with base in prism are exo deviations and base out are eso deviations.

Normal values and one standard deviation for the Von Graefe test are distance 1^{Δ} exophoria ± 2^{Δ}. At near the normal values are 3^{Δ} exophoria ± 5^{Δ} (Morgan, 1944a, Morgan, 1944b). Morgan suggested limits for results to be considered normal as the mean with a range either side of the mean of ± 0.5 SD as this would then include approximately 60-70% of the total population.

C.1.3 Modified Thorington (Hirsh and Bing, 1948 in Borish, 1970)

This test dissociates the eyes using a Maddox rod placed in front of one eye. A Maddox rod deforms a spot of light shone from the centre of the card into a coloured streak of light. The colour and orientation of the streak are determined by the colour of the material of the Maddox rod and the orientation of the lens. Patients view the Thorington card with the other eye. The card has horizontal and vertical lines with numbers on a scale (sometimes called a tangent scale). Two versions exist with numbers calibrated for use at either distance (6m) or near (40.5cm) (). Patients report which number the streak of light passes through. Results are recorded in prism dioptres. The test can be used to determine both horizontal and vertical phoria.

The modifications to the original Thorington test include using a Maddox rod instead of dissociating with prism and smaller target numbers on the chart to improve accommodative stimulus.

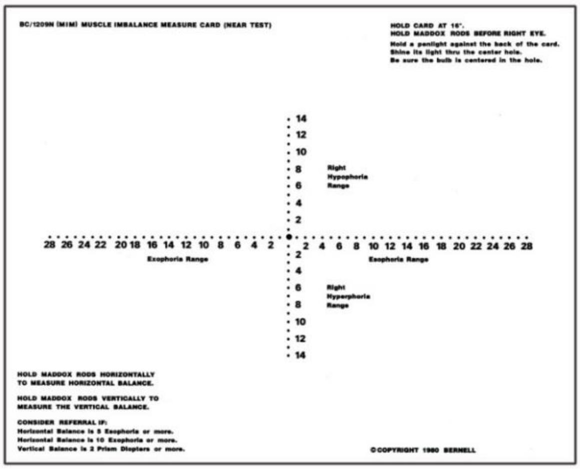

Figure C-1 Modified Thorington Near Chart (image from https://www.visus-sehteste.de).

C.1.4 Howell Phoria Chart (Wong *et al.,* 2002)

The Howell Phoria Chart includes a horizontal row of numbers with an arrow at the zero point. This test is carried out in free space with patients wearing their distance (or habitual distance) prescription. A dissociating lens of six prism dioptres base down in the right eye is used. The patient is asked to view the large Howell chart () at three metres and report the number on the bottom line nearest to the top arrow. The test is repeated at 33cm with the near phoria card. With six prism dioptres base down in the right eye, blue, even numbers indicate exophoria while yellow, odd numbers indicate esophoria. For near testing, the numbers should be clear to ensure accurate accommodation. The test card can be rotated to measure vertical displacement although this is seldom done in clinical practice. In addition, the large steps in the scale make the results less reliable for vertical phorias which are typically much smaller than horizontal phoria. Howell Phoria Card normal values are 0 (ortho) at 3m and mean 2^{Δ} exophoria ± 4^{Δ} at 33 cm (Wong *et al.,* 2002).

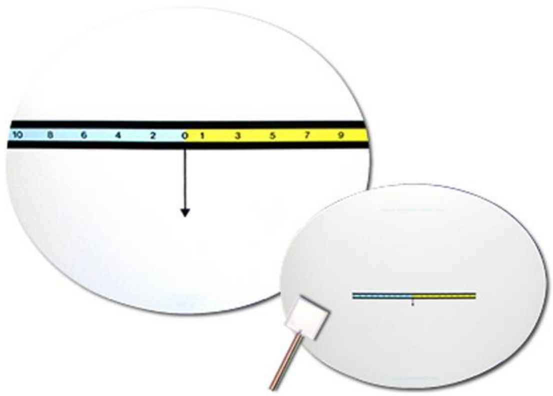

Figure AC-2 Howell Phoria Charts for measuring phoria at 33cm (right) and 3m (left). (image from http://www.optirepresentaciones.com.mx).

C.1.4.1 Limitations of phoria tests

Most of the tests measured here measure horizontal and or vertical deviations and not rotational (or cyclo-torsional) deviation. Each test of phoria gives slightly different results so that measurements made with one test cannot be directly compared with other tests (Wong *et al.,* 2002). Phoria results are influenced by whether the testing is done in free space or with a phoropter, the method used to dissociate, how well accommodation is controlled and the amount of proximal convergence (Schroeder *et al.,* 1996).

A study of the inter-observer repeatability for near phoria using the alternating cover test in children showed that there was good repeatability when the phoria was zero (orthophoria) (kappa = 0.76; 95% confidence interval = 0.75 to 0.83) or over 15 $^{\Delta}$ (kappa = 0.60; 95% confidence interval 0.56 to 0.65) but was poor for moderate phorias (kappa ranging from 0 to 0.19) (Garvey *et al.,* 2006).

One of the main limitations of dissociations tests is that they measure under the artificial condition of dissociation and have been found to be poor predictors of whether a phoria is compensated; and therefore, all dissociation tests are poor predictors of symptoms (Percival, 1928 cited in Evans, 2007). However dissociated tests still have value in being able to measure change in the vergence system.

Rouse and colleagues (2002) report good intra-examiner reliability in children 10 to 11 years old within and between testing sessions with the Von Graefe method. However, the Von Graefe method has been found to have poorer repeatability than the Modified Thorington test in adults (Casillas and Rosenfield, 2006).

Additional limitations of these tests include that dissociation tests can not differentiate between phoria and tropia so they need to be used in association with the cover-uncover test for accurate diagnosis. Also, some patients with strabismus suppress one eye which can produce anomalous results.

C.2 Fixation disparity tests

Heterophoria is the amount of misalignment of the eyes when the eyes are disassociated and see two separate images. In contrast, fixation disparity is a measure of the small misalignment of the eyes while viewing a target that is, in the most part, fused (Sheedy, 1980). The prism required to correct the misalignment is termed the associated phoria or aligning prism.

C.2.1 Saladin card

The Saladin Card is a relatively new testing card that includes a fixation disparity test (). Patients wear polarised glasses and are asked to view the card at 40cm from the eyes. A pen torch is held behind the card to illuminate the circles. Patients report which circle has lines that are perfectly vertically aligned and the value is recorded from the card. Vertical fixation disparity can be also measured.

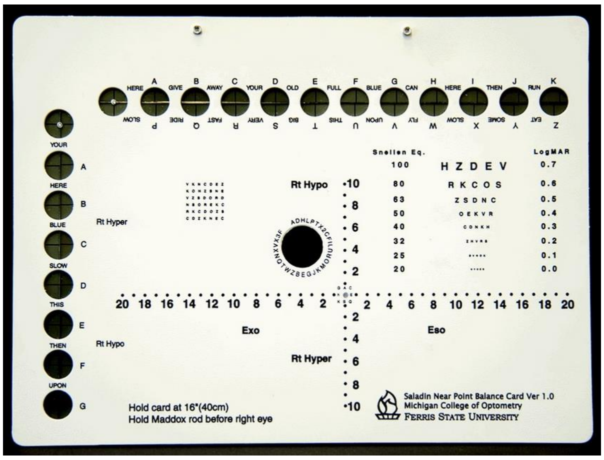

Figure AC-3 Saladin fixation disparity card (image from Franz *et al.,* 2011).

C.2.2 Sheedy disparometer

Patients view linear targets through polarised lenses so that each image is visible with one eye only (). Fusion is maintained through a para-foveal fusion lock that is slightly raised above the measuring lines. The lines are adjusted until they appear aligned to the patient.

While Frantz and colleagues (2011) found similar results with this test compared to the Saladin card, others have found the results of this test to be more variable than other measures of fixation disparity (Wildsoet and Cameron, 1985, Pickwell *et al.,* 1988, Alhassan *et al.,* 2015, Alhassan *et al.,* 2016).

Figure AC-4 Sheedy disparometer (image from Franz *et al.*, 2011).

C.3 Fusional reserves

Fusional reserves measure the ability to maintain single vision while moving target images with prisms. The test can be performed at distance and near (typically 40cm) with the eyes in primary position. Prism is introduced slowly either with rotary prisms through the phoropter or in free space with a prism bar (jump vergence). Accommodation is maintained by using a small target close to the limits of resolution.

Fusional reserves are measured with gradually increasing base out prism in front of both eyes to determine convergent ability or positive fusional reserves (eyes turning in toward the nose). With base in prism the divergent ability or negative fusional reserves are determined (eyes turning away from the nose). The patient reports if the target becomes blurred (blur point) or double (break point). After the break point, the power of the prism is reduced until the target returns to single vision (recovery point). Each of these points is recorded in prism dioptres. Testing can also be carried out for vertical vergences.

C.3.1.1 Limitations of fusional reserve tests

The findings of these tests are influenced by the level of effort of the patient, fatigue, and the speed of adjustment of the prism, type of prism stimulus (e.g., prism bar or rotary prism), target design, field of view, and probably test instructions. In addition, due to vergence adaptation, there is an order effect in that the reserve that is measured first will influence the reserve that is measured second. Rosenfield (1997) argues that the reserve that opposes the phoria should be measured first. Occasionally some patients are unable to perceive double vision and report one image moving which indicates suppression. Using a prism bar in free space allows the practitioner to observe the patient which in some cases allows the practitioner to determine when the eyes stop making a vergence movement.

C.4 Accuracy of the accommodative response (lag of accommodation)

As the accommodative demand increases by moving targets closer to the eye, the relative accommodative response falls off, and the eye becomes increasingly defocussed. This error of accommodation is called lag of accommodation when the accommodation falls behind accommodative demand. In some patients at near vision testing the accommodative response is excessive compared to the accommodative demand which is called a lead or spasm of accommodation. The main clinical approaches to measuring accommodative error will now be summarised.

C.4.1 Cross cylinder technique (Borish, 1970)

Patients view a cross pattern of horizontal and vertical lines () through a cross cylinder lens (usually ± 0.50D) with the minus cylinder axis located vertically (90 degrees) while wearing either their full distance correction or their habitual correction.

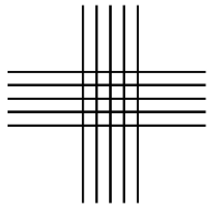

Figure AC-5 Fused cross cylinder target.

With this lens in place a perfectly clear image is not possible, while convergence is fixed so the eyes will take up a focussing position based on convergence. If a patient focuses precisely at the target distance, then the circle of least confusion (the midpoint between the two focal lines of the cross cylinder) will fall on the retina. With the circle of least confusion on the retina, horizontal lines will focus in front of the retina (myopic focus) and vertical lines will focus behind the retina (hyperopic focus) so that both set of lines will be equally blurred. If the accommodation is inaccurate, then one or the other set of lines will be clearer. Spherical lenses are introduced based on which lines are clearest until the horizontal and vertical lines are equally blurred. It is assumed that the amount of spherical lens correction required indicates the lag (positive spherical lenses) or lead (negative spherical lenses) of accommodation (see section 0).

The test is performed under dim lighting conditions to minimise the impact of the eyes' depth of focus. This is because in dim illumination the pupil dilates and there is less depth of focus with a dilated pupil.

Accommodative lag can be measured under monocular conditions to determine the accommodation driven by blur and proximal stimuli. Under binocular conditions the accuracy of accommodation to blur, proximal and convergent accommodation stimuli is assessed.

C.4.2 Dynamic retinoscopy

Several methods of dynamic retinoscopy have been described to give an objective measure of the accuracy of accommodation at near. Sheard (1920, cited in Borish, 1970) first demonstrated the inaccuracy of accommodation to near targets with retinoscopy so that at any given distance patients would accept a small amount of plus power. While he considered a small lag to be normal, a level above a small amount would indicate under-correction of the distance refraction, presbyopia or an anomaly of accommodation.

C.4.3 Monocular estimate method retinoscopy (Borish, 1970)

Patients view binocularly a detailed near target on the retinoscope typically at 40cm. Positive lenses are introduced briefly (for about 0.5 seconds) in front of one eye so as not to stimulate accommodation. The lag of accommodation is taken where the reflex seen with a retinoscope is neutral during the brief movement of the retinoscopy reflex of the eye through the introduced lens.

C.4.4 Nott retinoscopy

Patients focus on a near target typically at 40cm. The examiner moves forward and back with the retinoscope until the reflex is neutral. Movement of the examiner away from the patient indicates a lag of accommodation. The inverse of the working distance at which the neutral reflex is found is the magnitude of the accommodative response. The lag is the accommodative demand (inverse of the target distance) minus the accommodative response. This test has the advantage of not having to introduce correcting lenses that may influence the result.

C.4.5 Badal accommodative stimulus

Many automated instruments designed to measure the refraction and accommodation of the eye use a Badal lens system. The system uses a target and a positive lens is placed at its focal distance from the eye (the Badal Lens). The result of this set up is that the image size of the target is not affected by the target position. In addition, the target luminance is unaffected by the position of the target. Refraction is linearly related to target position. Test targets can be moved to various working distances to stimulate accommodation without the addition cues of altering target size or illumination. The testing is carried out monocularly so does not assess the accommodative-convergence response.

C.4.5.1 Limitations of lag of accommodation tests

A limitation of the cross-cylinder technique is that the patient may prefer clear vision in one meridian only and therefore have a preference for either horizontal or vertical lines, making determination of an endpoint difficult.

Benzoni and colleagues (2009) found that the cross-cylinder technique does not measure accommodative response accurately and the introduction of lenses required to perform the measurement causes a significant change in the accommodative response.

Dynamic retinoscopy using the monocular estimates method has limitations. In practice it is difficult to achieve the level of speed to eliminate an accommodative response as it is very brief (around 350 milliseconds) (Campbell and Westheimer, 1960, Hogan and Gilmartin, 1984). Locke and Somers (1989) and Jackson and Goss (1991) did not find any differences in results using the monocular estimate method compared to Sheard's technique which is essentially the same as the monocular estimates method but does not require the quick introduction of lenses.

The accommodation response to closed-view instruments using a Badal lens system is not equivalent to the response to a real target in space (Aldaba *et al.,* 2017) and therefore may not accurately reflect how the eye functions normally.

Accuracy of accommodation has been shown to vary when tested monocularly or binocularly, with the testing method, testing distance and with age (Nakatsuka *et al.,* 2003, McClelland *et al.,* 2004). In addition, the accommodative response is influenced by phoria measurements (Shor, 1999).

Mean lag of accommodation in young adults using the monocular estimate method at 40cm is +0.35 ± 0.34D (Cooper, 1987) or 0.33D in children and young adults (Tassinari, 2002). McClelland and colleagues (2004) found mean accommodative lag in children aged four to 15 years to be +0.30 ± 0.39D with a 4.00D accommodative stimulus using the Nott technique.

Intra-examiner repeatability was found to be better with the Nott retinoscopy and binocular cross cylinder technique compared to the monocular estimate method and autorefractor in adults (Antona *et al.,* 2009).

C.5 Positive and negative relative accommodation

Positive and negative accommodation represents the ability of the eyes to induce and relax accommodation while the vergence demand is fixed at near. Borish (1970) postulated that as the accommodation is increased with negative lenses, the accommodative convergence is also increased. Single vision is maintained by the use of negative fusional vergence. Once the limit of fusional vergence is reached the patient either experiences blur or diplopia. Similarly, with positive lenses to relax accommodation, accommodative convergence is also reduced. This is compensated by the positive fusional reserves.

A test target with letters close to the limit of resolution is held at (typically) 40cm. Patients wear their full distance correction (Borish, 1970). Negative lenses are introduced in 0.25D lens steps to induce accommodation until the patient reports blur. The result is recorded as the difference in power from the distance refraction.

Limitations of positive and negative relative accommodation tests

These tests require patients to determine first blur, which can be interpreted differently by different patients. The results can also be influenced by fatigue and the willingness to perform the test.

Normative values for mean positive relative accommodation are −2.37 ± 1.12D and +2.00 ± 0.50D for negative relative accommodation (Morgan, 1944a, Morgan, 1944b).

C.6 Accommodative facility (Flippers) (Evans, 2007)

The ability of the eye to make step jumps in accommodation is measured using accommodative facility testing. Testing can be performed monocularly, where it is used to determine the speed of the blur driven accommodative response or binocularly where it is used to alter accommodation while maintaining a fixed vergence.

Near accommodative facility is typically performed at 40cm using a near chart with a small letter target. Positive and negative lenses are introduced alternately using 'flippers'. Testing is usually done with ±2.00D lenses in the flippers, however smaller powers or different working distances may be used if the patient has difficulty with the initial lens power. Patients are instructed to report when the letters are clear, and then the lens is 'flipped' to the opposite direction until the letters are again reported as clear. One cycle is complete when both positive and negative lenses are cleared. The cycles are repeated for one minute and the results are recorded as cycles per minute.

Distance accommodative facility is measured using plano and −2.00D lenses. Patients wear their full distance correction. A letter chart is placed at distance (typically 6m) and patients are instructed to report when the letters are clear. Minus lenses are introduced and patients are once again to report when the letters are clear. One cycle is complete when both plano and negative lenses are cleared. The cycles are repeated for one minute and the results are recorded as cycles per minute.

Clinically additional information may also be recorded including difficulty with one of the lens conditions or a decrease in speed of cycles with time.

As this test is carried out with pre-fabricated flippers the centration distance is not matched to individual patients. Depending on patients' inter-pupillary distance additional fusional demand may be required to perform this test.

In experimental conditions, the time of individual flipping can be recorded using more accurate timer devices linked to the flipping device.

Normal response for ±2.00D flipper lenses at near is 7.7 ± 5 cycles per minute in young adults binocularly. Monocular values are right eye 11.6 and left eye 11.1 ± 5 cycles per minute (Zellers *et al.*, 1984). The high standard deviation values of this test highlight the large variability that can be found with this test.

McKenzie and colleagues (1987) found that participants who initially had good monocular and binocular accommodative facility also had good test-retest repeatability. However, those participants with initially reduced accommodative facility improved significantly with 60% reaching normal values over 3 visits. Similar results were found by Zellers and colleagues (1984) indicating a significant learning effect with repeated testing.

Scheiman and Wick (2014) include normative data for monocular and binocular facility including differences expected depending on age. Accommodative facility reaches young adult levels by the age of 13 years ().

	Accommodative facility (cycles per minute)	
Age (years)	**Monocular** (mean ± SD)	**Binocular** (mean ± SD)
6	5.5 ± 2.5	3.0 ± 2.5
7	6.5 ± 2.0	3.5 ± 2.5
8	7.0 ± 2.5	5.0 ± 2.5
13−30	11 ± 5.0	8.0 ± 2.5

Table AC-1 Normative values for accommodative facility at different ages (from Scheiman and Wick, 1994).

C.7 The accommodative convergence to accommodation (AC/A) ratio

The relationship between accommodation and accommodative convergence is considered to be relatively constant in individuals. (Borish, 1970) A change in accommodation at a fixed working distance is usually associated with a proportional change in accommodative convergence. This change can be determined by measuring dissociated phoria with variable amounts of accommodative demand. The change in phoria indicates the amount of accommodative convergence associated with accommodation. The relationship is expressed as a ratio (the AC/A ratio) with the change in accommodative convergence in prism dioptres divided by the change in accommodative demand in dioptres. While several methods for measuring AC/A exist, the most common method is the gradient method.

C.7.1 Gradient method (Borish, 1970)

A dissociated phoria is taken at near with a typical testing distance of 40cm. A lens of known amount (for example, −2.00D) is introduced and the deviation is retested. AC/A ratio can be obtained by plotting a graph of the introduced sphere versus the change in angle of deviation. However, because this is time consuming practitioners tend to estimate the AC/A ratio by recording the difference in phoria in prism dioptres divided by the lens value in dioptres.

Changes in the AC/A ratio with accommodative demand may be due to the eye's depth of focus, an accommodative response greater than or less than the demand (lag or lead of accommodation) and possibly a change in AC/A ratio.

C.7.1.1 Limitations of AC/A ratio tests

As this test may be performed using pre-fabricated flipper lenses, error in results may occur if the patient's inter-pupillary distance is different to the centration distance of the lenses. This error will be larger with the ±2.00D lenses than the ±1.00D lenses.

The technique used to determine phoria in AC/A ratio has been shown to give significantly different mean values and have different co-efficient of repeatability in young adults. Ratios obtained using the Modified Thorington technique with ±1.00D lenses showed the best repeatability (Escalente and Rosenfield, 2006). Mean value for gradient AC/A ratio has been found to be 3.49 ± 2.17D using a Howell card at 33cm in pre-presbyopic participants (Bhoola *et al.,* 1995).

C.8 Amplitude of accommodation

The amplitude of accommodation is the maximum amount of accommodation that the eye can achieve. Amplitude of accommodation is the difference in accommodation from the far point (relaxed accommodation) to the near point (accommodation fully exerted). Amplitude of accommodation is measured in dioptres. It can be measured monocularly and binocularly. There are several tests of amplitude of accommodation including the push-up method, the push down method and the minus lens technique.

Amplitude of accommodation can be influenced by general health, race, fatigue, previous exertion, medications, and age; the amplitude of accommodation decreasing significantly as patients age (Burns *et al.,* 2014). Other confounding factors in measuring amplitude of accommodation include the depth of focus of the eye, the ability to converge, the ability to recognize blur, the lighting conditions, target size, speed of moving the target (Evans, 2007) and the eye position (either up or down). For a comprehensive review see Burns and colleagues (2014).

C.8.1 Push-up test

Patients wear their full distance correction. A small target is moved towards the patient until they notice first blur. The target size should be close to the limit of resolution. This distance is measured (in metres) and the inverse of this is the dioptric value of accommodation. As the target moves closer the accuracy of accommodation decreases, although the depth of the focus of the eye means the image remains clear for longer than is accomplished by the actual accommodation would allow.

C.8.2 Push-down test

Patients wear their full distance correction. A small target is moved away from the eye until the patient first notices clear vision and this distance is measured (in metres). Again, the amplitude of accommodation is the inverse of this distance (measured in dioptres).

C.8.3 Minus lens technique

Patients wear their full distance correction. A small target is held at a fixed distance from the eye. Negative lenses are introduced in front of the eye until first noticeable and sustained blur. The amplitude of accommodation is the sum of the lenses introduced and the accommodative demand of the target working distance (typically +2.50D). This test can only be performed monocularly because if lenses are introduced binocularly the results are confounded by the eye's ability to fuse with fixed convergence.

Limitations of amplitude of accommodation tests

The angular subtense of the target increases with decreased working distance in these methods except the minus lens technique.

Normal values of amplitude of accommodation based on average values determined by Duane (1912) were estimated by Hofstetter (Borish, 1970) to be for the push-up test:

Amplitude of accommodation (D) = 18 – 1/3 age in years ± 2.00D.

In young adults, the minus lens test has been shown to have better repeatability than the push up or push down tests. The push up test gives higher values than the minus lens and push down tests. A change of ±1.50D is considered significant (Rosenfield and Cohen, 1996, Antona *et al.,* 2009).

In children aged four to 12 years, amplitude of accommodation varied by up to 5.20D with re-testing. Those children with initially poor amplitudes of accommodation significantly improved on retesting without training (Adler *et al.,* 2013).

C.9 Stereopsis

Stereopsis is the integration of the images of both eyes into a single image with the perception of depth. Testing can be done with 'contour stereopsis' where two similar images are separated laterally. Each eye views one image only with the use of polarised images and polarised spectacles. The Titmus Stereo test uses this ‘local’ (contours present) method. An alternate method is ‘global’ stereopsis. This method contains randomised dots that are visible by each eye separately and so there are no monocular cues. The Randot stereotest used in study 1 uses both types of stereoacuity.

Appendix D Expected values for accommodation and vergence testing (from Cooper *et al.*, 2011)

Measurement	**Mean**	**S.D.**	**Range**
Distance:			
Phoria	1X	2X	0-2X
Base-in blur	—	—	—
Base-in break	7	3	5–9
Base-in recovery	4	2	3–5
Base-out blur	9	4	7–11
Base-out break	19	8	15–23
Base-out recovery	10	4	8–12
Near:			
Phoria	3X'	5X'	0–6X
Base-in blur	13	4	11–15
Base-in break	21	4	19–23
Base-in recovery	13	5	10–16
Base-out blur	17	5	14–20
Base-out break	21	6	18–24
Base-out recovery	11	7	7–15
PRA	-2.25	0.50	-1.75 – +2.25
NRA	+2.00	1.1	+1.75 – 2.25
Gradient AC/A	4/1	2	3–5
AA	16 – (0.25 × age)	±2.00	±1.00

*Modified from Morgan MW. Analysis of clinical data. Am J Optom 1944; 21:477-91.

AA = amplitude of accommodation; AC/A = accommodative convergence/ accommodation ratio; NRA = negative relative accommodation; PRA = positive relative accommodation; X = exophoria at distance; X' = exophoria at near.

Appendix E Myopia Clinic questionnaire

Optometry and Vision Science
THE UNIVERSITY OF NEW SOUTH WALES

MYOPIA CLINIC QUESTIONNAIRE

This questionnaire will provide us with important information on genetic and environmental factors which may contribute to your myopia (short-sightedness). It will guide us in the management of your myopia including minimising the risk of further myopia progression.

Please complete this questionnaire to the best of your ability prior to your appointment. Any information provided in this questionnaire is strictly confidential.

PERSONAL INFORMATION

1. Name: ______________________ ______________________

   (First name) *(Last name)*

2. Date of birth: _______/________/_______

   (Day) *(Month)* *(Year)*

3. Gender *(please tick)*: ☐ Male ☐ Female

4. Country of Birth: ______________________________________

5. Grade at School: ______________________________________

6. Ethnicity *(please tick)*:

☐ Caucasian (European) ☐ Middle Eastern

☐ East Asian ☐ Indigenous Australian

☐ Indian/Pakistani/Sri Lankan ☐ South American

☐ African ☐ Unsure

☐ Melanesian/Polynesian ☐ Other *(please specify)*: ______________________

FAMILY HISTORY

7. Are any of your biological family members myopic (short-sighted)?

	Diagnosed at what age?	Prescription details?
☐ Mother		
☐ Father		
☐ Siblings		
☐ Siblings		

PREVIOUS EYE HISTORY

8. Do you wear glasses or contact lenses to correct your eyesight?

☐ Yes ☐ No *(go to question 14)*

9. At what age were you diagnosed with myopia (short-sightedness)? ______________________

10. How often do you wear your glasses or contact lenses? *(please tick)*

☐ All the time ☐ Most of the time

☐ Sometimes ☐ Rarely

11. Have you ever received one or more of the following treatments for myopia? *(please tick)*

☐ Bifocals ☐ Progressive lenses (multifocals)

☐ Atropine eye drops ☐ Orthokeratology

☐ Bifocal/Multifocal contact lenses ☐ Other (please specify):_______________________

12. Do you have your old glasses? *(if yes, please bring to the consultation)*

☐ Yes ☐ No

13. Do you have a copy of your previous prescription? *(please bring to consultation)*

☐ Yes ☐ No

14. Name of your primary eye care practitioner? ____

VISUAL ACTIVITIES

15. How many hours do you read on average in a day?_______________________

16. What type of lighting is normally used when you read or do close work? *(you may tick more than one box)*

☐ Desk Lamp ☐ Ceiling or room light

☐ Natural light (e.g. sunlight through window, skylight)

☐ Other *(please specify)*:_______________________

17. How long do you continuously read or do close work before taking a break of 5 mins or more?

☐ 0-15 minutes ☐ 16-30 minutes

☐ 31-45 minutes ☐ 45-60 minutes

☐ > 60 minutes

18. Please tick the average number of **hours per day** that you spend doing the following activities.

	On a week day				**On a weekend**			
Activity	None	<1hr	1-2hrs	≥3hrs	None	<1hr	1-2hrs	≥3hrs
Outdoor leisure activities (BBQs, picnic, beach, walk)	☐	☐	☐	☐	☐	☐	☐	☐
Playing outside (in a backyard, at the park, riding a bike)	☐	☐	☐	☐	☐	☐	☐	☐
Outdoor leisure activities (BBQs, picnic, beach, walk)	☐	☐	☐	☐	☐	☐	☐	☐
Watching TV/DVDs	☐	☐	☐	☐	☐	☐	☐	☐
Playing video games (e.g. Playstation)	☐	☐	☐	☐	☐	☐	☐	☐
Playing with toys, hobby or craft	☐	☐	☐	☐	☐	☐	☐	☐
Cooking, making or constructing things	☐	☐	☐	☐	☐	☐	☐	☐
School homework	☐	☐	☐	☐	☐	☐	☐	☐
Reading books for pleasure	☐	☐	☐	☐	☐	☐	☐	☐
Playing musical instruments	☐	☐	☐	☐	☐	☐	☐	☐
Using a computer or playing computer games	☐	☐	☐	☐	☐	☐	☐	☐
Playing handheld computer games (e.g. Nintendo DS, iPad)	☐	☐	☐	☐	☐	☐	☐	☐
Playing with and caring for pets	☐	☐	☐	☐	☐	☐	☐	☐
Going shopping								

19. Please tick any extracurricular/sporting activities you participate in, and whether these are undertaken outdoors, in a hall or gym, or in a classroom setting.

			Location		
Activity	Yes	Number of hours per week spent on activity	Outdoors	In a hall of gym	In a classroom
Dancing, gymnastics or martial arts	☐		☐	☐	☐
Athletics	☐		☐	☐	☐
Swimming	☐		☐	☐	☐
Football, soccer, rugby, league, AFL	☐		☐	☐	☐
Netball, basketball	☐		☐	☐	☐
Tennis or racquet sports	☐		☐	☐	☐
Cricket, golf	☐		☐	☐	☐
Skating, cycling, riding a scooter, rollerblading	☐		☐	☐	☐
Baseball/softball	☐		☐	☐	☐
Attending a youth group/club e.g. cubs, brownies etc	☐		☐	☐	☐
Other, please describe below	☐		☐	☐	☐
Attending a religious centre	☐		☐	☐	☐

Please list other activities:

____

____

____

____

Thank you for completing this questionnaire. If you have any questions regarding the questionnaire or our clinic please contact our clinic on the number below.

Myopia Clinic

UNSW Optometry Clinic

Level 1, Rupert Myers Building (North Wing)

School of Optometry and Vision Science

The University of New South Wales

Sydney, NSW, 2052

Acknowledgements: QUT Myopia Clinic

Appendix F Myopia Clinic Lifestyle modifications for myopia control

Optometry and Vision Science
THE UNIVERSITY OF NEW SOUTH WALES

LIFESTYLE MODIFICATIONS FOR MYOPIA CONTROL

Near work

- ***Take a 5 minute break for every 30 minutes of reading, drawing, studying and playing games (handheld or computer) -*** children who spend greater than 30 minutes continuously reading without taking a break tend to develop myopia more frequently than those children who took a break from reading every 30 minutes or less
- ***Use the distance from your shoulder to your elbow as a guide to how far you should be from your book when you are reading and writing, and the computer screen -*** children who read close to their work (30 cm or less) have a 2.5x greater chance of becoming myopic than those who sit further from their work
- ***Make sure you spend equivalent time reading and spending time outdoors (e.g. if you spend 1 hour reading a book, spend 1 hour outside) -*** children who spend more time, or those who read 2 or more books per week have a greater chance of becoming highly myopic than those do less reading.
- ***Read and study in a well lit room and have plenty of light on your page -*** some research shows that having a dark environment is more likely to make you become myopic

Outdoor Activity

- ***Increase daily time spent outdoors (e.g. walk to school, walk the dog, sit outside at lunch) as this can help reduce changes of developing myopia*** – recent research has shown that spending time outside, not necessarily sport, that protects our eyes from myopia.
- **Slip Slop, Slap, Seek, Slide! -** always use a hat, sunscreen, wrap around sunglasses and seek shade when you are outdoors.